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EVALUATION OF A MOUSE TEST FOR THE STANDARDIZATION OF THE IMMUNIZING POWER OF ANTI-RABIES VACCINES¹

By KARL HABEL, *Assistant Surgeon, United States Public Health Service*

The ideal animal test for the standardization of any vaccine should be done under conditions either similar to or at least comparable to those under which the vaccine is used clinically in human beings. The technique of performing the test should be simple and there should be no procedure in which individual differences of the technician might cause variation in results. The time required to complete a test is of practical importance since the material being tested cannot be released for clinical use until successfully meeting the requirements. Therefore the duration of the test should be sufficiently short so as not to subtract materially from the life of the vaccine. Results should be unequivocal and subject to but one interpretation. On repetition of identical tests the results should be uniform. The test animals used should be easily available, inexpensive, and easily cared for in the laboratory. The material used in testing the immunity produced by the vaccine must be uniform in its effect and in its potency, or the test must be so arranged that any changes in these properties will be revealed in the results. These are the requirements of the ideal test.

Since rabies vaccine was first used it has been subjected to many types of experimental tests to determine its immunizing properties and, therefore, its efficacy in the Pasteur treatment of human beings. This subject has been reviewed recently by Webster (1), who emphasizes the general lack of positive results in the light of statistical analysis of the published protocols.

In general, the following types of tests have been used.

1. *Injection of rabies virus into central nervous system (subdural, intracerebral, intraocular) followed by a course of vaccine treatment (1).*—In this method results have been quite consistently negative, the same mortality usually occurring among the vaccinated and control animals. This is easily understandable, since the direct introduction

¹ From the Division of Biologies Control, National Institute of Health.

of virus into the central nervous system produces the disease so rapidly that there is not sufficient time for a subsequent course of vaccine to produce immunity.

2. *Injection of rabies virus peripherally (intramuscular, subcutaneous, dog bite) followed by a course of vaccine treatment (1).*—This, of course, is the ideal method from the standpoint of simulating clinical conditions. Webster (1) has reviewed 98 such experiments and finds only 6 which show a significant degree of immunity. Besides the low percentage of positive results, there are several other disadvantages. First, rabies street virus must be used and the mortality even of control animals receiving such virus peripherally is extremely variable. Further, street virus strains vary considerably in their infectivity and even one strain will not be uniform over a long period for repeated testing since the animal passage necessary for maintaining it also changes its characteristics. The danger of laboratory infection of technicians in vaccinating animals which may be developing street virus rabies must also be considered. And, finally, there is the possibility of contaminating the rabies vaccine by mixing the brains of animals used to carry the street virus with those used for fixed virus. This would be of particular significance in those laboratories producing the live virus types of vaccine.

3. *Injection of virus into central nervous system subsequent to a course of vaccine treatment (1).*—The chief objections to this method are, first, that it does not simulate the clinical use of rabies vaccine in human beings and, second, that virus injected directly into the central nervous system is too severe a test, often bringing down all control and vaccinated animals.

4. *Injection of virus peripherally subsequent to a course of vaccine treatment (1).*—This method is closer to clinical conditions, but here the objections to street virus are again valid since most of these tests have used some street virus strain in the test dose. Several authors, however, have used fixed virus, or at least passage virus, as the test dose material with good results (2, 3, 4). There apparently is difficulty, however, in determining the M. L. D. by this method, the end point in titering the test virus being less definite than when titered intracerebrally. Another disadvantage would seem to be the greater possibility for individual differences in technique in an intramuscular as compared to an intracerebral injection.

5. *Development of virus neutralizing antibodies in serum of vaccinated animals.*—The titer of neutralizing antibodies in the serum can be determined after an immunizing course of vaccine and this has been suggested as evidence of the immunizing power of the vaccine by some authors (5). However, it has been shown in experimental animals that there is no direct relationship between serum antibody titer and the degree of actual immunity (6).

6. *Statistical review of human mortality rates in vaccinated individuals* (7).—Human mortality rates in vaccinated individuals obviously furnish an inaccurate estimate of the immunizing power of any vaccine since the degree of infection and often the definite diagnosis of rabies in the biting animal is not known. Also, the mortality rate in the persons bitten but not vaccinated is usually not available as a control. However, such a method is of no interest in the development of a standardizing test for rabies vaccines before their release for human use, which is the problem being considered here.

The monkey, dog, guinea pig, rabbit, rat, and mouse have all been used as experimental animals in tests of the immunizing power of anti-rabies vaccine. The expense and difficulty of obtaining large numbers of uniform animals rules out the routine use of the monkey and the dog. If the experiments are conducted in such a way as to attempt to determine the number of M. L. D.'s resisted by the vaccinated animals, then the number required would probably eliminate the guinea pig, rabbit, and perhaps the rat for the same reasons. For practical purposes the mouse would seem to be the best animal and it is known to be quite susceptible to rabies infection. For this reason the experiments here reported have been limited almost exclusively to the investigation of an immunity test in mice.

The mouse technique has been developed chiefly by Webster (4) at the Rockefeller Institute. In general, it consists of a series of intraperitoneal injections of vaccine followed by the test dose of virus injected either into the central nervous system or peripherally in serial dilutions.

INVESTIGATION OF LIMITATIONS OF MOUSE TEST

MOUSE FACTORS

(1) *Strain of mice*.—For uniform results in a biological test the use of animals of a pure strain is desirable because of possible variations in reactions of animals of different strains. The Swiss white mouse strain is now well established in this country as a pure strain well suited for biological work. It is easily available from most animal breeders and, as far as can be determined, the line has been kept pure. The mice used routinely in this laboratory are of this strain.

Groups of 25 female Swiss mice, 1 month old, from our own breeding department and purchased from three outside dealers were immunized with a vaccine (5 percent emulsion, 0.5 percent phenol) known to be highly immunizing. All mice were given 6 intraperitoneal doses of 0.25 cc. of a 1/10 dilution, each dose being given every second day. Fourteen days after the first dose of vaccine the test dose of fixed virus (heterologous strain) was injected intracerebrally in serial tenfold dilutions. The M. L. D. for each group was obtained by

setting aside 15 control mice at the start of the experiment and injecting them with the test dose dilutions.

Table 1 shows that there was rather close agreement as to the amount of protection (6,000 and 4,722 M. L. D.) between mice of substrains A and B, but that mice of substrains C and D showed 20,000 and 45,000 M. L. D. immunity, respectively. In seeking for an explanation of these discrepancies we found that, although supplied to us by outside dealers as 1-month-old mice, the mice from breeders C and D were apparently older than this, as shown by their average weights:

Substrain A-----	11 gm. average weight, 6,000 M. L. D. protection
Substrain B-----	11 gm. average weight, 4,722 M. L. D. protection
Substrain C-----	12 gm. average weight, 20,000 M. L. D. protection
Substrain D-----	15 gm. average weight, 45,000 M. L. D. protection

TABLE 1.—Ability of substrains of Swiss mice to be immunized by same rabies vaccine

Substrain of Swiss mice	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)							Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. Substrain A mice, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 6 doses. Test dose on 14th day:								
a. Vaccine No. 1-----	2/4	2/4	0/4	0/4	2/4			6,000 (1/600,000)
b. Controls-----					3/4	1/3	0/3	
II. Substrain B mice:								
a. Vaccine No. 1-----	4/5	1/6	2/5	2/5	2/5			4,722 (1/2,125,000)
b. Controls-----					4/4	3/5	1/4	
III. Substrain C mice:								
a. Vaccine No. 1-----	3/5	2/5	1/5	1/4	0/4			20,000 (1/1,400,000)
b. Controls-----					3/5	4/5	0/5	
IV. Substrain D mice:								
a. Vaccine No. 1-----	3/5	0/6	0/6	0/5	0/5			45,000 (1/900,000)
b. Controls-----					5/5	2/5	0/4	

¹ All 50 percent end points (see reference 10).

As will be shown in the next series of experiments reported in this paper, the degree of immunity produced by a vaccine increases with the age of the mice up to a certain point. In this experiment there was close agreement between the two groups of the same average weight and the degree of immunity increased with the weight of the mice in the other two groups.

(2) *Age of mice.*—Casals and Webster (8) have shown that the ability of mice to be immunized against rabies is proportionate to their age. At least they demonstrated a much greater immunity in 60-day-old as compared with 21-day-old vaccinated mice when tested with intramuscular post-vaccination virus.

Groups of female Swiss mice 1 month old (average weight 11 gm.), 2 months old (average weight 22 gm.), and 6 months old (average weight 24 gm.) were immunized with vaccine No. 1 of known high and vaccine No. 2 of known low immunizing power. They received 0.25 cc. of 1/10 dilution intraperitoneally every second day for 6 doses

and were injected intracerebrally with fixed virus dilutions on the fourteenth day. Controls at each age level were injected simultaneously with the test virus. Table 2 reveals that when immunized with vaccine No. 1, 1-month-old mice resisted 6,000 M. L. D., 2-month-old mice 16,666 M. L. D., and 6-month-old mice probably 200 M. L. D., although this is not so definite since the control dilutions were not carried out far enough to establish a definite end point. All age groups failed to develop demonstrable immunity with vaccine No. 2.

TABLE 2.—*Immunity produced by same vaccines in Swiss mice of different ages*

Age of mice	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)							Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. One-month-old mice, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 6 doses. Test dose on 14th day:								
a. Vaccine No. 1	2/4	2/4	0/4	0/4	2/4			6,000
b. Vaccine No. 2	5/5	4/5	5/5	3/4	4/5			Less than 10 (1/600,000)
c. Controls					3/4	1/3	0/3	
II. Two-month-old mice:								
a. Vaccine No. 1	2/3	0/4	1/4	1/3				16,666
b. Vaccine No. 2	2/2	4/4	3/4	2/2				Less than 100 (1/1,000,000)
c. Controls				4/4	4/4	3/4		
III. Six-month-old mice:								
a. Vaccine No. 1	3/5	3/5	2/5	2/4	1/4			200+ (?)
b. Vaccine No. 2	3/3	3/4	4/4	4/4	3/4			0
c. Controls			3/3	3/3	4/4			(1/100,000) (?)

(3) *Sex of mice.*—Two similar experiments were performed about 1 month apart. In both a group of 1-month-old male and an equal group of 1-month-old female Swiss mice were immunized. They received 0.25 cc. of 1/10 dilution of vaccine No. 1 intraperitoneally every second day for 6 doses. In the first experiment the test dose was given on the twenty-first day, whereas in the second experiment it was given on the fourteenth day.

TABLE 3.—*Influence of sex of mice on immunity produced*

Sex of mice	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)							Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. 0.25 cc. 1/10 dil. vaccine No. 1 intraperitoneally every 2 days for 6 doses. Test dose on 21st day:								
a. Female mice—								
1. Vaccinated		2/3	0/3	2/4	1/3	2/4		1,250 (1/1,000,000)
2. Controls					4/4			
b. Male mice—								
1. Vaccinated		4/4	4/4	0/4	0/4	0/4		100 (1/550,000)
2. Controls					4/4			
II. 0.25 cc. 1/10 dil. vaccine No. 1 intraperitoneally every 2 days for 6 doses. Test dose on 14th day:								
a. Female mice—								
1. Vaccinated	2/4	2/4	0/4	0/4	2/4			6,000 (1/600,000)
2. Controls					3/4	1/3	0/3	
b. Male mice—								
1. Vaccinated	3/4	1/4	3/4	2/4	0/4	3/4	0/3	1,000 (1/1,000,000)
2. Controls					2/4			

In the first experiment, as shown in table 3, the females resisted 1,250 M. L. D. as compared with but 100 M. L. D. for the males. In experiment 2 the females gave 6,000 M. L. D. protection and the males 1,000 M. L. D.

(4) *Number of mice on test.*—An important question in the test is the number of mice to be used in order to secure uniform results.

Two groups of 1-month-old Swiss mice were immunized by 10 doses of 0.25 cc. of 1/10 dilution, given intraperitoneally every second day, using vaccine No. 1 and vaccine No. 2. The test dose was given on the twenty-first day from the start of the vaccine in serial tenfold dilutions. Each group was subdivided so that the test was done in duplicate, one subgroup consisting of 3 mice receiving each dilution of the test dose and the other of 4 mice. In the two subgroups a total of 7 mice received each dilution.

Table 4 shows that for vaccine No. 1 the 50 percent end point was the same (at least 10,000 M. L. D. protection) whether 3, 4, or 7 mice were injected. However, with vaccine No. 2, when 3 mice were included there was protection against less than 10 M. L. D., against 550 M. L. D. when 4 mice were used, and against 314 M. L. D. when 7 mice were injected.

TABLE 4.—*Influence of number of mice tested on results*

Number of mice tested with each dilution of test virus	Test dose dilutions of fixed virus intracerebrally (Number rabies deaths/number tested)						Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	
I. Vaccine No. 1, 0.25 cc. of 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
a. 3 mice to a group.....	0/3	1/3	0/3	1/3	-----	-----	10,000+
b. 4 mice to a group.....	0/4	1/4	1/4	0/4	-----	-----	10,000+
c. 7 mice to a group.....	0/7	2/7	1/7	1/7	-----	-----	10,000+
II. Vaccine No. 2, 0.25 cc. of 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
a. 3 mice to a group.....	3/3	2/3	2/3	3/3	-----	-----	Less than 10.
b. 4 mice to a group.....	3/4	4/4	0/4	0/4	-----	-----	550
c. 7 mice to a group.....	6/7	6/7	2/7	3/7	-----	-----	314
III. Controls.....	-----	-----	4/4	4/4	3/4	0/4	(1/2,200,000)

VACCINE FACTORS

(1) *Percentage emulsion used in vaccine.*—Because of the amount of chemical (phenol, chloroform, formalin) in the undiluted vaccine, its use in that form in mice gives symptoms of and occasionally deaths from chemical intoxication. Therefore the vaccine must be diluted. Webster (4) dilutes all vaccines 1 to 10 regardless of the percentage of the original emulsion. For the usual 5 percent emulsion vaccine this represents, in the dose usually used for the mouse (Webster $\frac{1}{8}$ of human dose), approximately 18 times the relative dose by weight given to a 100-pound person. However, the mice receive but 6 doses as

compared with 21 doses in the human being. Mice thus receive but 6 times as much brain substance. Therefore, if the vaccine were diluted 1/60 or 1/50 it would more closely approximate the human dose by weight. Groups of 20 female Swiss mice 1 month old received 0.25 cc. of 1/10, 1/25, and 1/50 dilutions of the 5 percent phenolized vaccine No. 1, intraperitoneally, every second day for 6 doses. Twenty-one days from the start of the vaccination each group was subdivided into groups of 4 mice each and given, intracerebrally, serial tenfold dilutions of the test strain of fixed virus. They were observed for 21 days before being discharged. Table 5 shows the results. The 1/10 dilution of vaccine protected against 1,250 M. L. D.; the 1/25 and 1/50 dilutions gave immunity against 45 and 55 M. L. D., respectively.

TABLE 5.—*Influence of amount of vaccine injected on immunity produced*

Dilution of vaccine No. 1	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)						Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
0.25 cc. vaccine intraperitoneally every 2 days for 6 doses. Test dose on 21st day:							
1/10 dilution	2/3	0/3	2/4	1/3	-----	-----	1250
1/25 dilution	4/4	4/4	3/4	0/4	0/3	-----	45
1/50 dilution	4/4	4/4	2/4	1/4	0/3	-----	55
Controls	-----	-----	-----	4/4	2/4	0/4	(1/1,000,000)

(2) *Site of injection.*—Rabies vaccine is given subcutaneously to human beings, but within the limits of the doses practicable for the mouse even vaccines of known high antigenicity fail to produce demonstrable immunity when given subcutaneously to mice. Immunity is developed regularly when the same dose is given intraperitoneally. A further advantage of the intraperitoneal injection for routine testing is the relative resistance to infection with live virus given by that route when live virus vaccines are being tested.

(3) *Volume of vaccine per dose.*—Mice of 1 month of age can be given up to 0.75 cc. intraperitoneally, but 0.25 cc. is readily tolerated and has been used in all these experiments.

(4) *Number and interval of vaccine doses.*—Groups of 20 female Swiss mice 1 month old were immunized according to the following schedules, using both vaccine No. 1 and vaccine No. 2.

A----- 0.25 cc. of 1/10 dil., intraperitoneally, 1 dose.

B----- 0.25 cc. of 1/10 dil., intraperitoneally, every second day for 5 doses.

C----- 0.25 cc. of 1/10 dil., intraperitoneally, every day for 10 doses.

On the tenth day following the first dose of vaccine the mice were divided into groups of 4 and given the test dose strain of fixed virus intracerebrally.

TABLE 6.—*Influence of the number and interval of vaccine doses on degree of immunity*

Dosage schedule of vaccines	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)						Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. Vaccine No. 1:							
a. 0.25 cc. 1/10 dil. intraperitoneally, 1 dose.....	4/4	4/4	4/4	4/4	-----	-----	Less than 10.
b. 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 5 doses.....	3/4	1/4	2/4	2/3	-----	-----	800
c. 0.25 cc. 1/10 dil. intraperitoneally every day for 10 doses.....	4/4	1/4	1/4	1/3	-----	-----	1,600
II. Vaccine No. 2:							
a. 0.25 cc. 1/10 dil. intraperitoneally, 1 dose.....	4/4	4/4	4/4	4/4	-----	-----	Less than 10.
b. 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 5 doses.....	3/3	3/3	3/3	3/3	-----	-----	Less than 10.
c. 0.25 1/10 dil. intraperitoneally every day for 10 doses.....	3/4	4/4	4/4	3/3	-----	-----	Less than 10.
III. Controls.....	-----	-----	4/4	4/4	2/3	0/4	(1/1,600,000)

Test dose on tenth day.

The results, as shown in table 6, indicate that with both the vaccines of high and low antigenicity, no immunity could be demonstrated in 10 days in the groups receiving a single immunizing dose. When 5 doses every second day were given there was no immunity with vaccine No. 2 and 800 M. L. D. protection with vaccine No. 1. Ten daily immunizing doses with vaccine No. 1 protected against 1,600 M. L. D. but with vaccine No. 2 gave no protection.

TEST DOSE FACTORS

(1) *Street virus or fixed virus.*—The disadvantages of using street virus in routine testing over a period of time have been mentioned above. This experiment was designed to compare the degree of protection in mice immunized with vaccine No. 1 and vaccine No. 2 when tested by both street and fixed virus intracerebrally.

Groups of 16 female Swiss mice 1 month old received 0.25 cc. of 1/10 vaccine dilution intraperitoneally every second day for 10 doses. The test doses of fixed virus strain and of first guinea pig passage street virus (original dog brain virus) were given intracerebrally 21 days from the start of vaccine injection.

Table 7 shows that vaccine No. 1 protected against 10,000 M. L. D. of fixed virus and against at least 1,000 M. L. D. of street virus. Vaccine No. 2 protected against 461 M. L. D. of fixed virus and but 10 M. L. D. of street virus. The discrepancies here are understandable in view of the irregular results with the street virus even in the controls.

(2) *Number of M. L. D. in test dose dilutions.*—How closely can we determine the number of M. L. D. protected against in this type of test? In other words, by how much shall the serial dilutions of the test dose differ? A fairly large series of tests of this type have been done giving 1, 10, 25, 50, 100, and 200 M. L. D. to the groups of

vaccinated mice. With the levels of the test virus dilutions this close to one another there are frequently discrepancies and overlapping of groups so that a definite end point is difficult to determine. On the other hand, if tenfold serial dilutions are made this overlapping is, to a great extent, eliminated. Since the test dose virus titration is being done in the controls at the same time the test is being run in the vaccinated animals it is impossible to know exactly beforehand what the titer will be. However, if test virus passages are done in mice in the same manner the week before each test and the mice are killed at the same stage of fixed virus rabies, the brains kept in the cold (0° C.), and then emulsified the day the test dose is given, the titer will usually be the same each time.

TABLE 7.—Comparison of immunity to fixed virus and street virus intracerebrally

Groups tested	Test dose dilutions of fixed and street virus intracerebrally (number rabies deaths/number tested)						Number of M. L. D. protection (dilution = 1 M. L. D.)
	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	
I. Vaccine No. 1, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
a. Fixed virus test dose.....	0/3	1/4	1/4	0/4	-----	-----	10,000+
b. Street virus test dose.....	0/3	0/3	0/4	0/4	-----	-----	1,000+
II. Vaccine No. 2, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
a. Fixed virus test dose.....	3/4	4/4	0/4	0/3	-----	-----	461
b. Street virus test dose.....	3/3	2/4	0/4	0/4	-----	-----	10
III. Controls:							
a. Fixed virus.....	-----	-----	-----	4/4	3/4	0/4	(1/2,800,000)
b. Street virus.....	-----	-----	1/4	2/4	0/4	-----	(1/10,000)

(3) *Homologous vs. heterologous strain of fixed virus.*—In order to determine whether cross immunity exists between different strains of fixed rabies virus and, therefore, whether homologous virus may be used as the test dose, the following experiment was made.

Groups of 20 female Swiss mice 1 month old were vaccinated intraperitoneally with 6 doses of 0.25 cc. of 1/10 dilution of vaccine No. 1, each dose given every second day. Twenty-one days from the first dose of vaccine the following fixed virus strains were given intracerebrally as the test dose to the 3 groups:

Virus A.—Homologous strain, identical with that used to prepare vaccine No. 1, originally the Pasteur strain.

Virus B.—Heterologous strain, isolated from a rabid dog in 1935 and carried through approximately 80 intracerebral passages in mice.

Virus C.—Heterologous strain, isolated from a rabid skunk and carried through 170 intracerebral passages in mice.

A control group was inoculated with each fixed virus strain to determine its titer.

Table 8 summarizes the results. Homologous virus A demonstrated protection against 8,000 M. L. D., heterologous virus B against 1,250 M. L. D., and heterologous virus C against 10,000 M. L. D.

TABLE 8.—*Comparison of immunity tested by homologous and heterologous fixed virus*

Strain of test dose fixed virus	Test dose dilutions of fixed virus intracerebrally (number rabies deaths/number tested)							Number of M. L. D. protection (dilution=1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. Homologous virus A, 0.25 cc. 1/10 dil. vaccine No. 1 intraperitoneally every 2 days for 6 doses. Test dose on 21st day:								
a. Vaccinated.....	3/3	1/4	1/4	1/4	0/4	-----	-----	8,000
b. Controls.....	-----	-----	-----	4/4	4/4	1/3	-----	(1/800,000)
II. Heterologous virus B:								
a. Vaccinated.....	-----	2/3	0/3	2/4	1/3	-----	-----	1,250
b. Controls.....	-----	-----	-----	4/4	4/4	2/4	-----	(1/1,000,000)
III. Heterologous virus C:								
a. Vaccinated.....	0/3	2/4	1/3	2/4	-----	-----	-----	10,000
b. Controls.....	-----	-----	-----	4/4	2/4	4/4	-----	(1/1,000,000)

(4) *Diluent used for test dose.*—It has been shown by Milam (9) that rabies virus in high dilutions is readily killed in a short time at room temperature if the diluent is normal saline. Ten percent horse serum in distilled water kept the virus viable in high dilutions for the longest time and this has been used throughout these experiments. This is important where a large number of mice are being given the test dose, for if the procedure takes several hours the virus given to the final groups of mice may have a lower titer than that given at the start of the test.

(5) *Route of administration of virus.*—The choice here is between an intracerebral or a peripheral injection of test virus. Webster (4) has favorably compared results in mice by the two methods. However, the difficulty of determining a definite end point of the titer even in controls and the relatively small range of dilutions that are infective are disadvantages of the intramuscular test. Injected into the gastrocnemius muscle, as Webster recommends, the dose in mice is 0.01 cc. The difficulty of delivering exactly 0.01 cc. from an ordinary 0.25 cc. syringe, together with the fact that serial dilutions of the test virus are of but twofold differences (2, 4, 8, 16 M. L. D.) would seem to make the overlapping of groups quite likely and therefore make a definite end point of the number of M. L. D. protected against more difficult to determine.

To be sure, the intracerebral virus is a very severe test of immunity but it is reasonable to assume that a vaccine giving protection against the more severe test of virus given intracerebrally would likewise give protection against the less severe test of intramuscular virus.

(6) *Sources of error in technique.*—The possibility of error sufficient to affect the results of the test lies chiefly in the way in which the intracerebral injection is made. In the first place, the mouse must be anesthetized deeply enough so that the injection can be completed before the mouse begins to struggle. Second, the end of the needle must be in the substance of the brain. It is possible to insert the

needle too far and then the virus may be injected into the nasopharynx instead of intracerebrally. This can, in part, be prevented by using a short needle ($\frac{1}{8}$ to $\frac{3}{16}$ in.). The site of the injection is a little to one side of the midline, half the distance from eye to ear. The chief source of error in our experience has been due to leakage of the injected material through the opening in the skull left when the needle is withdrawn. This leakage by measurement has often amounted to 0.02 cc. of the 0.03 cc. originally injected. To overcome this a fine gauge, sharply bevelled needle should be used (27-gauge preferably). The injection should be slow enough to allow some diffusion of the material away from the needle tip. And, most important of all, the finger or thumb of the left hand holding the mouse's head during the injection should be placed over the site of the injection as soon as the needle is removed and light pressure applied for a few seconds.

(7) *Interval from start of immunization to test dose.*—Since the amount of time required for any test should be as short as possible in order that the product being tested may be released for use, it is important to determine the minimum number of days necessary for the immunized mice to develop demonstrable immunity.

Webster (4) has reported that mice given 1 intraperitoneal dose of an antigenic vaccine will show demonstrable immunity within 7 days. However, most workers have waited 21 or 30 days after the first dose of vaccine before giving the test dose.

Four groups of 16 Swiss mice 1 month old were immunized. Two groups received vaccine No. 1 and 2 vaccine No. 2. One of the 2 groups used for each vaccine received 0.25 cc. of 1/10 dilution, intraperitoneally, every day for 10 doses and was given the test dose intracerebrally on the tenth day. The other group was given 0.25 cc. of 1/10 dilution of vaccine intraperitoneally every second day for 10 doses and the test dose was given intracerebrally on the twenty-first day.

TABLE 9.—*Influence of time of test dose*

Groups tested	Test dose dilution of fixed virus intracerebrally (number rabies deaths/number tested)						Number of M. L. D. protection (dilution=1 M. L. D.)
	10 ⁻³	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	10 ⁻⁷	
I. Vaccine No. 1:							
a. 0.25 cc. 1/10 dil. intraperitoneally every day for 10 doses. Test dose on 10th day.....	4/4	1/4	1/4	1/3	-----	-----	2600
b. 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day.....	0/3	1/4	1/4	0/4	-----	-----	10,000+
II. Vaccine No. 2:							
a. 0.25 cc. 1/10 dil. intraperitoneally every day for 10 doses. Test dose on 10th day.....	3/4	4/4	4/4	3/3	-----	-----	Less than 10.
b. 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day.....	3/4	4/4	0/4	0/3	-----	-----	722
III. Controls:							
a. On 10th day.....	-----	-----	4/4	4/4	2/3	-----	(1/1,000,000)
b. On 21st day.....	-----	-----	-----	4/4	3/4	0/4	(1/2,600,000)

The results given in table 9 show that, with the highly immunizing vaccine, mice tested on the tenth day resisted 2,600 M. L. D. and those tested on the twenty-first day resisted at least 10,000 M. L. D. However, with mice immunized with the less immunogenic vaccine those tested at 10 days had no immunity, whereas those tested at 21 days resisted 722 M. L. D.

Using the same highly immunogenic vaccine No. 1, one month after the above experiment, a group of mice received 0.25 cc. of 1/10 dilution, intraperitoneally, every second day for 6 doses. They were tested on the fourteenth day (See Ia, table 2) and resisted 6,000 M. L. D.

(8) *Interval from test dose to discharge of mice.*—The time required for observation of the mice following the test dose adds greatly to the total time required for the mouse test. In a series of over 50 tests of immunity in mice, using fixed virus intracerebrally as the test dose and observing the mice for 30 days, it has been found that the average time of the last death is 15 days, with an occasional death up to 20 days. A death after 20 days of observation is exceedingly rare.

UNIFORMITY OF RESULTS

Any test of biological products should give the same results when done in duplicate.

Vaccine No. 1 was given in 10 doses every second day, 0.25 cc. of 1/10 dilution, intraperitoneally, to 2 groups of 1-month-old Swiss mice. The test dose was given intracerebrally on the twenty-first day. Table 10 shows that both groups resisted at least 21,000 M. L. D.

The same was done with vaccine No. 2, using 3 groups of mice. One of these groups showed resistance to 500 M. L. D., another resisted 21 M. L. D., and a third 55 M. L. D.

TABLE 10.—Results of duplicate tests

Groups tested	Test dose dilution of fixed virus intracerebrally (number rabies deaths/number tested)						Number of M. L. D. protection (dilution = 1 M. L. D.)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻⁴	10 ⁻⁵	10 ⁻⁶	
I. Vaccine No. 1, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
Group I.....	0/3	1/3	0/3	1/3	-----	-----	21,000+
Group II.....	0/3	1/4	1/4	0/4	-----	-----	21,000+
II. Vaccine No. 2, 0.25 cc. 1/10 dil. intraperitoneally every 2 days for 10 doses. Test dose on 21st day:							
Group I.....	3/4	4/4	0/4	0/4	-----	-----	500
Group II.....	3/3	2/3	2/3	3/4	-----	-----	21
Group III.....	3/4	3/4	3/4	2/3	-----	-----	55
III. Controls.....				4/4	3/4	0/4	(1/2, 100,000)

COMPARISON TO CLINICAL CONDITIONS

The closest approach to clinical conditions in experimental animals is the post-infection immunization method where street virus is given peripherally and then the vaccine is started.

A group of 36 guinea pigs weighing 250 to 300 grams was given 0.2 cc. of 1/10 centrifuged emulsion of original dog brain street virus in each masseter muscle. Thirty animals were started immediately on a series of 21 daily injections of 0.5 cc. of vaccine No. 1, which had been shown to produce a high degree of immunity in the mouse test. Three of the vaccinated and 1 control guinea pig died of infections other than rabies, 11 vaccinated guinea pigs died of rabies, while 16 survived, whereas 4 of the 5 controls developed rabies. The animals were observed for a period of 2 months and all deaths were checked by smears of Ammon's horn for Negri bodies to verify the diagnosis.

INTERPRETATION OF RESULTS

What should be considered the end point of protection in the mouse test? When results are clear-cut the end point may be taken as the greatest number of M. L. D. with which 50 percent of the mice survive. However, quite often the differentiation between groups representing the different numbers of M. L. D. is not so clear-cut. Then the method of Reed and Muench (10) for determining 50 percent end points should be employed for both control and vaccinated groups. By dividing that dilution representing the 50 percent end point of the controls into that of the vaccinated mice the number of M. L. D. protection is obtained.

Discussion

In view of the experimental results here reported, the recommended technique in the mouse test is as follows:

Thirty Swiss mice, all of one sex and preferably females, 1 month of age (11 to 13 grams) should be given 0.25 cc. of a 0.5 percent brain emulsion of the vaccine (1/10 dilution for 5 percent vaccine, 1/50 dilution for 25 percent vaccine, etc.), intraperitoneally, every second day for 6 doses. Eighteen control mice should be set aside at the start of the test. Fourteen days from the first dose of vaccine the test dose should be given to both vaccinated and control mice. In preparation for this at least 3 normal mice should be given 0.03 cc. of a 10 percent emulsion of the fixed virus strain about 7 days after the first dose of vaccine. These mice will then come down with fixed virus rabies just in time for the test dose. These 3 mice should be killed on the first day of definite symptoms and the brains should be removed and kept at 0° C. until used. On the fourteenth day these mouse brains

are emulsified at 1/10 dilution by weight with 10 percent horse serum in distilled water. The 10 percent emulsion is centrifuged at 1,000 r. p. m. for 10 minutes. The supernatant is then carried through serial tenfold dilutions from 10^{-1} to 10^{-7} . In order to determine the M. L. D. of the test virus the 18 control mice are divided into 3 equal groups and given, intracerebrally, 0.03 cc. of the 10^{-5} , 10^{-6} , and 10^{-7} dilutions. Groups of 6 vaccinated mice should be given 0.03 cc., intracerebrally, of the 10^{-1} , 10^{-2} , 10^{-3} , 10^{-4} , and 10^{-5} dilutions. These mice should be observed for 21 days and only those showing symptoms of fixed virus rabies before death should be considered as rabies deaths. The M. L. D. is the highest dilution given the control mice which causes death from rabies in at least 3 of the 6 injected mice. The end point of the immunity in the vaccinated mice is the lowest dilution of test dose virus in which at least 3 of the 6 mice tested survive. The number of M. L. D. protected against can be determined easily by the number of times the dilution giving the end point in the vaccinated mice is more concentrated than that in the controls. With irregular results 50 percent end points should be determined for control and vaccinated groups by the method of Reed and Muench (10).

The technique described is applicable with all the types of killed virus vaccines (phenolized, formalized, etherized, chloroform-killed, heat-killed, etc.) in which all the human doses are identical.

For those vaccines utilizing live or attenuated virus (Pasteur, Hogenes, Harris) the mouse test can also be used in a modified form. The 6 intraperitoneal injections given the mice must be graded so that each successive dose contains more and more virulent material, as is done in human vaccination with the same vaccines.

Having enumerated the requirements of the ideal test at the beginning of this paper we shall now examine the mouse test here recommended in relation to those specifications.

Although the test conditions are admittedly dissimilar to clinical conditions obtaining in the human use of rabies vaccine, we feel that we have demonstrated that a vaccine showing antigenic power by the mouse test will also be efficacious in the post-infection treatment of rabies, as shown in the experiment with guinea pigs. Or perhaps it would be more exact to state that a vaccine giving a high degree of immunity, as measured by the mouse test, will be of more value clinically than one giving less immunity in mice.

The technique is simple and, if a few precautions are observed in giving the intracerebral test dose, there is no procedure in which individual differences of the technician can cause appreciable variations in the results.

We feel that the time required for this mouse test (5 weeks) is as short as it is possible to make any test of rabies immunity, and it is certainly shorter than most tests used in the past.

Results are uniform in identical tests except in those vaccines giving but borderline immunity. This disadvantage may be overcome by making the required degree of immunity (number of M. L. D. protection) sufficiently high. Since the basis of determining the end point of the test is the death of mice with symptoms of rabies there should be no difficulty in interpreting results.

The test animals, Swiss white mice, are easily available, inexpensive, and easily cared for in the laboratory.

The test dose material is the same virus being carried for the production of vaccine and therefore will be uniform from one test to the next and any change in its virulence will be detected in the control mice where it is titrated each time the test is performed.

How many M. L. D. protection by the mouse test is necessary for a vaccine to be of value in clinical use? At present this question cannot be answered definitely. However, in view of the possibility of irregular results in those vaccines giving but a small degree of immunity and the fact that some vaccines are capable of protecting against as high as 50,000 M. L. D., immunity against at least 1,000 M. L. D. in the mouse test should be considered the minimum requirement of an efficient rabies vaccine.

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HELIUM-OXYGEN MIXTURES FOR ALLEVIATION OF TUBAL AND SINUS BLOCK IN COMPRESSED AIR WORKERS¹

By J. W. CROSSON, *Assistant Surgeon (R)*, ROY R. JONES, *Surgeon*, and R. R. SAYERS, *Senior Surgeon, United States Public Health Service*

The Division of Industrial Hygiene of the National Institute of Health, United States Public Health Service, conducted a field study

¹ From the Division of Industrial Hygiene, National Institute of Health.

on compressed air illness at the Queens Midtown Tunnel in New York City from July 1938 to May 1939, in cooperation with the United States Bureau of Mines, the New York Tunnel Authority, and the Walsh Construction Co. During the course of this study a by-product of the investigation was developed which has gained increasing interest in the field of compressed air work. Inasmuch as the publication of the formal bulletin will be delayed for some time it was suggested that the work done on helium-oxygen mixtures for relief of tubal and sinus block be produced in a separate article, which is accordingly presented here.

Helium-oxygen mixtures have been suggested for the treatment and prophylaxis of compressed air illness almost since the time of recognition of the properties of helium. J. C. McLennan (1) stated that the use of this gas in conjunction with oxygen was suggested by Elihu Thompson for divers so that "the period of submergence as a consequence might be considerably increased." Charles Cooke (2) in 1923 was granted a patent for the use of helium with oxygen for divers, based on the fact that helium has a coefficient of solubility approximately one-half that of nitrogen and because it is twice as diffusible. Sayers, Yant, and Hildebrand (3) in 1925 stated: "Helium is without odor or taste and has physical properties which promise to be of interest physiologically and which have been found to have possibilities of great practical use, especially in making a synthetic atmosphere that will reduce the hazard of caisson disease. The substitution of helium for the nitrogen ordinarily present in the air we breathe has been found to result in an atmosphere which is as respirable as that provided by nature. The results obtained indicate that helium not only has the advantage of being less soluble than nitrogen, but also has the advantage of diffusing more rapidly in the body fluids and tissues which results in rapid elimination of the gas from the tissues during decompression."

Sayers and Yant in 1926 (4) gave a more comprehensive account of their work which indicated the efficacy of helium in preventing compressed air disease, in shortening decompression time, and showed the safety of its use. The physiologic properties and the therapeutic application of helium have been demonstrated by Behnke and Yarbrough (5) and by A. L. Barach (6). Helium has never been used for ordinary decompression in caisson or tunnel work, however, since the cost is prohibitive. It is used in diving operations, although to no great extent as yet, being limited usually to dives of great depth or of long duration, and chiefly by the United States Navy. Edgar End (7) in 1938 reported a fresh-water dive of 420 feet with the use of an 80-percent helium and 20-percent oxygen mixture during which there were no toxic symptoms manifest and following which no symptoms of compressed air illness were noted.

Work in this direction was not pursued in this field study since the amount of helium necessary to carry on an experiment of such large proportion would be almost out of the question, and because pure oxygen could be used with no danger at the pressures under which the men were decompressed (8, 9). The report regarding decompression of compressed air workers using pure oxygen will be published at a later date.

An effort was made, however, to relieve that condition known in compressed air work as "ear block." This subjective complaint of pain or discomfort in the ears is a distinct entity encountered in compressed air work and entirely separate from that known as compressed air illness. It was first described in detail by Armstrong and Heim in 1937 (10), who observed the condition in aircraft pilots. They suggested the term *aero-otitis media* and defined it as "an acute or chronic traumatic inflammation of the middle ear caused by a pressure difference between the air in the tympanic cavity and that of the surrounding atmosphere, commonly occurring during changes of altitude in airplane flights and characterized by inflammation, discomfort, pain, tinnitus, and deafness." The condition which they described and toward which they directed attention as a new clinical entity is identical with the changes observed in compressed air workers suffering from "ear block."

Detailed description of the anatomy and normal and special physiology of the middle ear and eustachian tube indicated that *aero-otitis media* is due to lack of ventilation of the middle ear, and is caused by failure or inability to open the eustachian tube voluntarily when necessary.

The same authors (10) also listed the objective signs of this condition. These are essentially the same as those observed in affected compressed air workers. "The objective signs depend on the amount of trauma sustained. In mild cases the drum may appear normal except for a moderate degree of bulging or retraction when a small amount of pressure differential still persists. An increased pressure in the tympanic cavity is denoted by a bulging of the tympanic membrane with a loss or decrease of the light reflex.

"A negative pressure in the tympanic cavity is denoted by a retraction of the tympanic membrane with a decrease in size and brilliance of the light reflex and an increased prominence of the short process of the malleus with a foreshortened and more horizontal handle.

"Following more severe trauma the drum may be retracted or bulging as already described, and in addition there is also an inflammation, which in appearance varies from a slight pink tinge to an angry red. In all cases the inflammation is most marked along the larger vessels

that follow the malleus handle and around the drum periphery. When the inflammation is severe it cannot be distinguished from acute infectious otitis media and has frequently been mistaken for it.

"Traumatic ruptures of the tympanic membrane are usually linear and quite extensive. * * *"

The chronic phase of aero-otitis media is also seen in compressed air workers and is described by Armstrong and Heim (10) as follows: "The drum membrane is dull, lusterless and slightly thickened and the light reflex is diminished or absent. Hearing acuity is diminished either unilaterally or bilaterally and in the latter case there is usually a considerable difference between the two sides."

In compressed air workers the condition might advance to a frank otitis media if relief of the block is not afforded promptly. The acute condition might also regress within a few hours.

The ears, however, may not be involved, but an obstruction of one or more of the ostia of the accessory nasal sinuses may produce a severe pain in the area of the affected sinus. The only objective sign in sinus block may be a small amount of bleeding from the nose. If relief from this condition is not afforded, the pain continues and an acute sinusitis is likely to develop. Tubal and sinus blocks are most commonly encountered in workers with upper respiratory infection, while the tubal block² is more common in workers in apparently good health.

The eustachian tube is a ventilating shaft and drainage canal from the middle ear to the posterior pharynx. It is normally collapsed but in acts such as swallowing or yawning the dilator muscles with which it is supplied contract and the tube is opened. Thus, without any conscious effort, the air pressure on either side of the tympanic membrane is kept in equalization at all times. Another means of opening this tube is to use the Valsalva method, that is, to close the nose and mouth tightly and to attempt to expire forcefully, thus increasing pressure in the pharynx and forcing air up to the middle ear via the eustachian canal.

In "locking in" the compressed air worker must consciously or unconsciously continuously equalize the pressure in his accessory sinuses and middle ear. Some of the workers appear to be doing nothing to equalize this pressure, but in these cases it will usually be noted that they hold their lower jaws in a slightly extended position, and hold their tongues away from the roof of the mouth and posterior or soft palate. In this way they dilate the eustachian tube slightly and the air readily passes up to the middle ear. Many of the workers

² The terms tubal and sinus block are preferred in this instance because it is primarily the "block" which precipitates the sinusitis or the condition described by Armstrong and Heim. It is the purpose of the apparatus described later to forestall an aero-otitis media or sinusitis by relieving the "block." It is felt that treatment of the traumatic or infectious inflammation should proceed at present along already well-established methods of therapy.

swallow while locking in, but the majority use the Valsalva method. These men enter the tunnel in gangs of 30 to 50 in number and if one man acquires a "block," the intruding air must be shut off at once, and the pressure is usually lowered. Then a second try is made, and if not successful this time, the worker must leave the lock. This, of course, necessitates the return to normal pressure by the whole gang. This "bouncing up and down," or fluctuation of the pressure often precipitates a "block" in one or more men of the gang attempting recompression after the first worker has been "locked out." In addition to being time consuming and wasteful of the compressed air, it is very trying on the men themselves.

Oftentimes, rather than lose a shift or be ridiculed by his mates, a worker will "force himself through," that is, he will endure the pain and discomfort in the hope that it will right itself in a short time. These are the cases which are more prone to develop an otitis media, often with subsequent suppuration. These cases, too, are the ones in which rupture of the ear drum may occur.

Let us now follow the worker who was "locked out." He blows and snorts and goes through various contortions, at the end of which his head may or may not feel clearer. If the man lock is not yet available, he will usually attempt to get into the tunnel through the muck lock in which the pressure is raised and lowered with great speed since only materials for construction are supposed to pass through. Here again he runs a chance of developing a suppurative otitis media or a ruptured tympanum. Sometimes he attempts to go through the emergency lock, but this is used frequently and may not be available, or he may not know how to manipulate the controls. Here, too, if he is not careful a rupture of the drum may occur, because the emergency lock is small and the pressure increases rapidly unless the controls are handled with skill.

The regulations imposed by the contractor's physician request the worker to return to the surface and to the medical dispensary immediately after being "locked out" for a "block." However, he usually does not do this until all other methods have failed, chiefly because of the distance between the man lock and the dispensary, and the time involved in travelling back and forth. If he does report to the physician on duty, a series of shrinking solutions will be placed far back in his nose and throat, which may or may not be efficacious in breaking the block.

During this study a method of eliminating these conditions was tried out. Helium is the lightest of all the elements except hydrogen; it is inert and can be used safely as a component of a respirable gas. Lovelace and Mayo (11), in February 1939, described a treatment for alleviation of aero-otitis media in which a helium-oxygen mixture was used. With reference to the velocities of the molecules under

discussion they stated: "The rate of diffusion of helium is 2.7 times that of nitrogen. The mean velocity of the oxygen molecule at 0° C. and a pressure of 760 mm. Hg is about 0.425 km./sec., of the nitrogen molecule 0.453 km./sec., and of the helium molecule 1.202 km./sec." It is probable, therefore, that in a respirable gas mixture composed of oxygen and helium, the latter should diffuse through an accessory nasal sinus ostium or the eustachian tube more rapidly than would the nitrogen of air. Thus the equalization of pressure between the middle ear and the external barometric pressure should occur more readily.

The mucous membrane lining the upper respiratory passages is a delicate tissue. It is sensitive to environmental or atmospheric and physiologic changes and is subject to infection with all its concomitant phenomena. Mild inflammation and congestion are therefore not uncommonly noted in an otherwise healthy individual. Under ordinary atmospheric conditions, equalization of pressure between the accessory nasal sinuses and the middle ear with the external atmosphere is accomplished with little or no difficulty. If there is a rapid change in external atmospheric pressure, however, it seems reasonable to assume that the rapid influx of air and the increased pressure upon the ostia and tubal openings might cause a puckering of the congested and boggy mucous membrane of these entrances and so produce a valve-like block. The presence of a thick mucoid discharge might also be an added factor of mechanical obstruction. As the external pressure is increased, there is a negative pressure produced in the cavities which draws the walls of the openings together and further aids in the exclusion of the outside air. The natural warning of such a situation is the occurrence of pain in the affected ear or sinus. It should be recalled that any change in atmospheric pressure is transmitted immediately to the blood stream. The pain probably arises from the distention of the blood vessels supplying the membrane lining the cavity which is now under a negative pressure, that is, a pressure less than that of the blood vessels themselves. When a tubal block occurs, pain is also caused by stretching of the ear drum owing to increased or decreased external pressure. Should the negative pressure within the cavity be maintained, natural forces will be set in motion to equalize the pressure with that of the external atmosphere. Since immediate equalization is not possible by means of a gaseous medium, attempts at equilibrium will be made by means of a liquid medium brought about by extravasation of blood or serum into the cavity with the negative pressure. The presence of free blood or serum in an area accessible to, or in which there may be pathogenic organisms, favors the development and progress of infection.

A return to the original atmospheric pressure will permit the establishment of former conditions and the ostia and openings might again

become patent. If the condition has been maintained for too long a time or if too vigorous methods have been applied to break the block, the openings may remain closed and gas interchange and fluid drainage will not be possible.

It should be noted that the above described phenomena may take place when the external atmospheric pressure is either raised or lowered, except that extravasation of blood or serum is not likely to occur in the lowering of the external pressure. The cavity in that case will be under increased pressure and pain will be caused by the pressure of the expanding gases within the cavity against the mucous membrane lining. The occurrence of tubal or sinus block is infrequent when the external pressure is lowered because (1) decompression is usually performed with less speed than compression, and (2) the anatomy of the involved parts facilitates the exit rather than the entrance of gases.

If a respirable mixture of helium and oxygen is breathed after the ostia and tubal openings have re-established their patency, the lungs and upper respiratory passages will become filled with the new mixture. When a change in atmospheric pressure is now attempted, puckering, closure, and adhesion of the openings will be less probable for two reasons: (1) The establishment of a state of equilibrium between the helium-oxygen filled cavities and the nitrogen-oxygen gas mixture of the outside atmosphere will now become necessary; and (2) the speed of the helium molecule, which is 2.7 times that of nitrogen, will aid the forces operating to bring about this equilibrium. In addition to the employment of voluntary methods, therefore, the operation of forces demanding an equilibrium of the gaseous mixtures will bring about an equalization of pressure in the tympanic cavity and accessory nasal sinuses.

A simple apparatus was designed by the United States Bureau of Mines Laboratories which could be used by the worker in the man lock. It consists of a small cylinder of 80 percent helium and 20 percent oxygen connected through a small reducing valve to a "lung" or breathing bag adapted from a 2-hour self-contained oxygen breathing apparatus frequently used in mine rescue work. The breathing bag is equipped with an admission valve which is automatically tripped when the bag collapses. Attached to the bag is a rubber tube on the end of which is a detachable face mask. The whole apparatus is no larger than a small suitcase and can be left permanently in the man lock in charge of the lock tender.

Because this apparatus was not immediately available a temporary one was constructed by utilizing an oxygen breathing apparatus of a type used in mine rescue work, but exhaling to the outside air and attaching to a large cylinder of the helium-oxygen mixture. A small detachable face mask was substituted for the full face mask of the

original machine. This apparatus was too large and unwieldy to remain in the man lock and was placed in the checker's shanty just outside. Its use still necessitated the return to normal pressure. The "locked out" worker could breathe this mixture and after he had breathed it two minutes or less, the lock tender could return for him and take him on through. In this way a series of 84 recorded cases were treated, 82 of which were able to re-enter the tunnel and to continue their work with no discomfort or danger to themselves.

Two cases of this series failed to respond sufficiently to pass through the lock; one was a worker who had been out of compressed air for 2 weeks and who was suffering from a subacute pansinusitis and the other was one of our own staff who had never had any experience in compressed air before and who had a chronic catarrhal sinusitis. In the latter instance no attempt was made to break the "block" by means of the helium-oxygen mixture until 30 hours after its occurrence.

When the smaller apparatus was available it was placed in the hands of the contractor for use in the man lock. Individual cases were not recorded at this time and no accurate record of results is available. This method can probably be made more efficient and practicable than keeping the apparatus outside the lock. When a "block" occurs while the gang is "locking in," the air is shut off and the pressure is reduced a pound or two. The apparatus is automatic and ready for instant use. No manipulation is necessary once the machine is set. The affected worker applies the mask and breathes normally for one minute or a little more, and usually the "block" is broken. He can then go on through either still using the mask or not as necessity demands.

This procedure should save considerable time, both for the worker and the employer, in addition to obviating the danger and discomfort of the disabling tubal or sinus block.

In "locking out," a "block" is not so likely to occur, but occasionally it does. Here, too, the same method may be used. A few inhalations of the helium-oxygen mixture permits decompression to continue in the regular manner.

SUMMARY

1. Some of the physical and physiologic properties of helium have been enumerated, together with a reference to the safety of its use in prevention and prophylaxis of compressed air illness.
2. A description is given of another entity encountered in compressed air work known as "ear block," more properly termed tubal or sinus block.
3. The occurrence of tubal or sinus block as observed in the compressed air worker and the conditions which promote this occurrence are described.
4. The theory of the mechanism of "block" and its alleviation by means of helium is explained.

5. A new and simple apparatus as designed by the United States Bureau of Mines Laboratories is presented for the relief of tubal and sinus block by administration of 80 percent helium and 20 percent oxygen.

6. The use of this apparatus in the man lock itself is strongly urged in order to prevent the occurrence of more serious complications of "block." Also, this will obviate the necessity of fluctuation of pressure which frequently precipitates a "block" in one or more men attempting recompression after the first worker has been "locked out."

7. The use of an improvised apparatus in the field study produced results indicating a high degree of efficacy in the prevention of tubal and sinus block. Experience with this apparatus also indicated that once the "block" is complicated by inflammation, from whatever cause, the helium-oxygen administration is not likely to be effective, and that complications following "block" should be treated by well-established therapeutic measures.

8. It is suggested that with limited instruction to the workers the use and value of this apparatus will be recognized, since manipulation is unnecessary and the results are rapid and convincing.

ACKNOWLEDGMENTS

Acknowledgment and deep appreciation are accorded to Mr. F. E. Griffith and Mr. H. A. Watson of the United States Bureau of Mines for their invaluable work in the development and use of the apparatus herein described; to Dr. Edward Levy of the Port of New York Authority for his suggestion regarding the development of an apparatus for alleviation of tubal and sinus block; to Dr. G. C. Emory for permitting the use of the new apparatus on employees under his care and for his helpful suggestions throughout the study; to members of Local 147, Compressed Air, Tunnel, Caisson, Subway, Cofferdam, and Sewer Construction Workers Union; and members of the engineering staff of the New York Tunnel Authority who submitted to the new method of treatment. The apparatus used by the contractor on this study was constructed by the Mines Safety Appliances Company, of Pittsburgh, with suggestions for design by the United States Bureau of Mines Laboratories.

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TWO EPIZOOTICS OF PLAGUE INFECTION IN WILD RODENTS IN THE WESTERN UNITED STATES IN 1938

By L. B. BYINGTON, *Surgeon, United States Public Health Service, Plague Suppressive Measures Laboratory, San Francisco, Calif.*

In the course of field investigations of plague during the summer of 1938, two small outbreaks of considerable intensity involving wild rodents were observed. One occurred in Lincoln County, Wyo., the other in Catron County, N. Mex. The Wyoming outbreak appeared to be a direct extension of the disease from infected animals in nearby Idaho and Utah. The New Mexico epizootic took place more than 150 miles from any other known plague-infected region.

PLAGUE INFECTION IN LINCOLN COUNTY, WYO.

Lincoln County is situated on the western border of the State and adjoins both Idaho and Utah. The surface is a rough, rocky, and sandy intermountain plateau covered with sagebrush. Most of the land is not inhabited, but there are a few narrow fertile valleys utilized for farming and some grazing land. Coal mining is the chief industry. There are nearly as many persons engaged in mining as in agriculture. Most of the population is distributed along the Union Pacific Railroad and U. S. Highway 30N. in the southern third of the county, and it was here that the plague infection in rodents was observed. The principal towns are Kemmerer, a mining center and railroad division point, with a population of 1,834; Diamondville, near Kemmerer, with a population of 812; and Cokeville, near the Idaho boundary, with 431 inhabitants. The population density for the entire county is 2.5 persons per square mile, but must be considerably greater in the area under discussion.

Early in July 1938 the personnel of a mobile laboratory investigating plague infection in that region were advised of an unusual mortality in ground squirrels in the vicinity of Cokeville. Residents reported that, 3 or 4 weeks previously, dead ground squirrels had been seen in an

abandoned sheep corral 6 miles north of that town. Investigation revealed the presence of plague infection in Uinta ground squirrels (*Citellus armatus*), Wyoming ground squirrels (*Citellus richardsonii elegans*) and woodchucks (*Marmota flaviventris*). Between July 2 and August 12, 1938, 37 plague-infected rodent specimens were obtained from a total of 115 specimens taken; i. e., 32.2 percent of the specimens were plague infected. All were taken from an area approximately 40 miles square. At the same time 12 additional plague-positive specimens were taken from scattered adjacent areas not included in this report. The distribution of plague in the rodent hosts is given in table 1.

It will be observed that these numbers refer to specimens and not to individual animals. A specimen represents from 1 to 150 rodents of the same species collected at one time from one locality from which the ectoparasites were pooled for subsequent guinea pig inoculation. By this procedure a specimen found to be plague infected was assumed to contain only one infected animal, although it is possible that several of the rodents contributing to a specimen may have been infected. Specimens consisting of only one animal were limited to this number because the autopsy findings suggested plague in that particular rodent. Eighteen of the 37 plague-positive specimens consisted of only one animal. The range in the number of animals per specimen is indicated by table 2.

TABLE 1.—Distribution of plague in rodent hosts, Lincoln County, Wyo., 1938

Animal	Number of specimens	Number plague infected	Number negative	Percent infected
Uinta ground squirrel (<i>Citellus armatus</i>).....	56	31	25	55.3
Wyoming ground squirrel (<i>Citellus richardsonii elegans</i>).....	29	5	24	17.3
Woodchuck (<i>Marmota flaviventris</i>).....	7	1	6	14.3
Prairie dog (<i>Cynomys leucurus</i>).....	23	0	23	0
Total.....	115	37	78	32.2

TABLE 2.—Median and average numbers of animals included in one specimen of rodents, Lincoln County, Wyo.

Animal	Plague-positive specimens		Plague-negative specimens	
	Median	Average	Median	Average
Uinta ground squirrel (<i>Citellus armatus</i>).....	15	29	40	43
Wyoming ground squirrel (<i>Citellus richardsonii elegans</i>).....	31	35	15	16
Woodchuck (<i>Marmota flaviventris</i>).....	1	1	12	17
Prairie dog (<i>Cynomys leucurus</i>).....	0	0	2	2

The geographic distribution of the plague-infected rodents in the area described is shown in figure 1. Most of these animals were shot

or found dead in the rural or desert districts, but some were obtained from urban areas and one plague-infected rodent was killed on a golf course.

The course of the epizootic is indicated by figure 2. Although the chronologic distribution of the series somewhat resembles a normal curve, information indicates that the outbreak had been in progress for several weeks before any animal samples were obtained. The parasite-host relationship was investigated and will be reported later. There were no cases of plague in man.

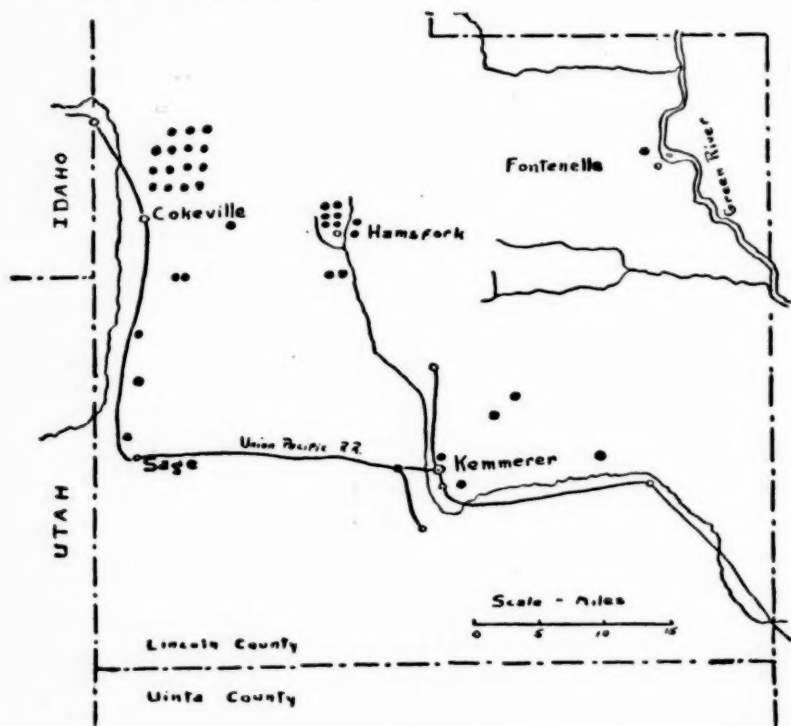


FIGURE 1.—Map of part of Lincoln County, Wyo., showing distribution of plague-infected rodent specimens obtained in 1938.

PLAGUE INFECTION IN CATRON COUNTY, N. MEX.

Catron County is situated on the western border of the State, midway from north to south. The southern part of this county consists of high, rugged mountains; the northern part is a desert mesa. The county is thinly populated, having an area of 7,042 square miles and a population in 1930 of 3,282, or a density of 0.4 persons per square mile. Fewer than 800 persons in the county are engaged in farming. The largest town is Mogollon, with a population of 295. Reserve, the county seat, has 206 inhabitants.

In April and May 1938 Mr. J. C. Gatlin, of the United States Biological Survey, noted an unusual mortality in prairie dogs in northern Catron County and reported that fact to the Plague Suppressive Measures Laboratory of the Public Health Service in San Francisco, Calif. The collection of specimens was begun in that area on August 6, and between that date and September 26, 23 plague-infected specimens were obtained from a total of 49 secured. The distribution of this infection, by hosts, is given in table 3, and the variation in size of the samples is shown in table 4.

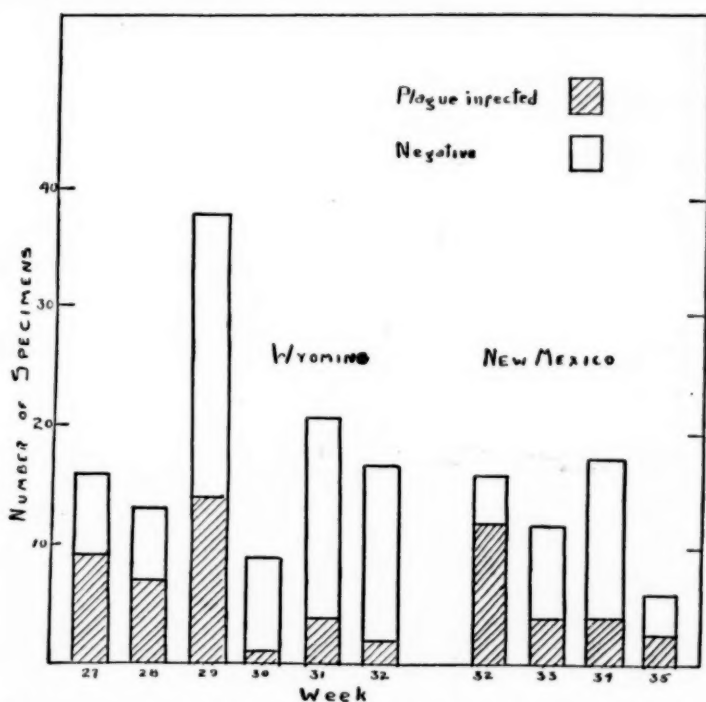


FIGURE 2.—Frequency of plague-infected specimens in total number of specimens of wild rodents obtained in Lincoln County, Wyo., and Catron County, N. Mex., in 1938, by weeks.

TABLE 3.—Distribution of plague in rodent hosts, Catron County, N. Mex., 1938

Animal	Number of specimens	Plague infected	Number negative	Percent infected
Say's rock squirrel (<i>Citellus variegatus grammurus</i>).....	6	1	5	16.6
White footed mouse (<i>Peromyscus truei truei</i>).....	1	1	0	100.0
Zuni prairie dog (<i>Cynomys gunnisoni zuniensis</i>).....	42	21	21	50.0
Total.....	49	23	26	46.9

TABLE 4.—Median and average numbers of animals included in one specimen of rodents, Catron County, N. Mex.

Animal	Plague-positive specimens		Plague-negative specimens	
	Median	Average	Median	Average
Say's rock squirrel (<i>Citellus variegatus grammurus</i>).....	1	1	1	1
White footed mouse (<i>Peromyscus truei truei</i>).....	1	1	0	0
Zuni prairie dogs (<i>Cynomys gunnisoni zuniensis</i>).....	1	6	11	11

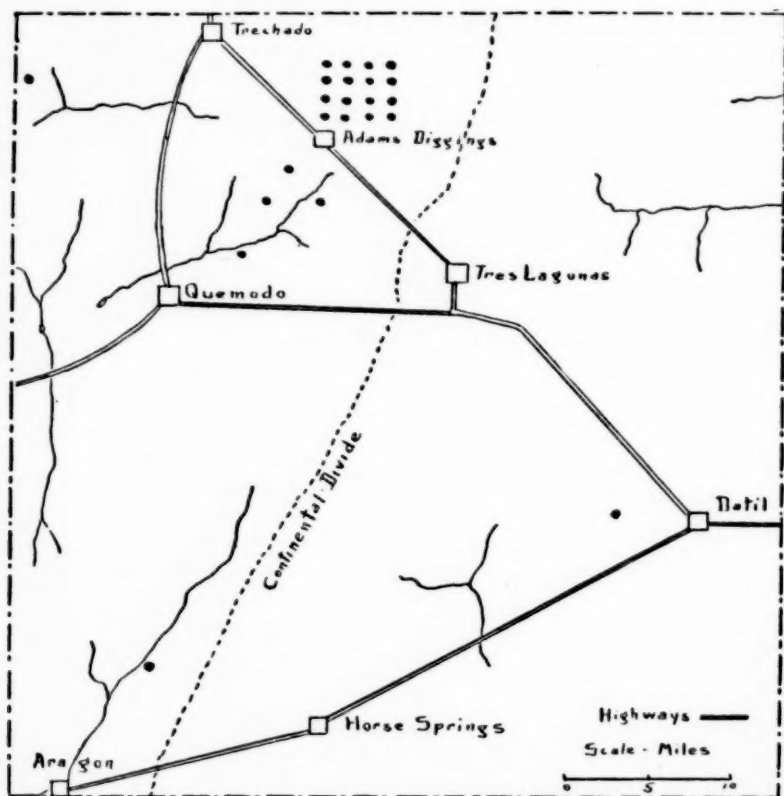


FIGURE 3.—Map of part of Catron County, N. Mex., showing distribution of plague-infected rodent specimens obtained in 1938.

It will be observed that plague infection was found in nearly one-half of the samples collected.

The chronologic course of the outbreak is suggested in figure 2. The declining course of the curve resembles that of the terminal portion of an epidemic and it is known that this study was not begun until several months after unusual rodent mortality was observed. Apparently this epizootic started in April and continued until the end of September.

The geographic distribution of the infection is shown in figure 3. No human cases of plague were reported in connection with this

epizootic. One year after this outbreak, a resurvey of this region was made. No plague-infected animals were found at this time in the area originally found infected but several plague-positive specimens were taken from Valencia County, north and west of Catron County, suggesting the gradual spread of enzootic plague in that direction.

Two years after the epizootic another study failed to demonstrate any infected animals in that part of the State.

CONCLUSION

Epizootic outbreaks of plague in rodents are occurring in the western United States. These are part of a widespread enzootic of the disease in many species of rodents. The two outbreaks here reported took place in regions sparsely inhabited by man and no human cases were known to have been associated with the infection in rodents.

(NOTE.—The surveys in 1938 and 1939 were performed under the supervision of Senior Surgeon Clifford R. Eskey, who was at that time in charge of the Plague Suppressive Measures Laboratory. The field work was supervised by Passed Assistant Surgeon V. H. Haas and Assistant Surgeon Wixom Sibley.

CARE OF THE EARS AND PREVENTION OF DEAFNESS¹

General Statement.

Comparatively few people are aware of the extent of the problem of deafness.

The results of examinations of school children indicate that about 15 percent, or one in every six or seven children, has some impairment of hearing. Conservative investigators state that about half of these children (6 percent) suffer serious hearing loss. It has been estimated that one-third of all adults have some deafness in one or both ears. In this connection, it is highly important for the public to realize that the majority of causes which lead to deafness are preventable.

The working parts of the organs of hearing are delicate structures and, if they are to function efficiently, must be given competent care.

Parts of the Ear.

The *external ear*, or *pinna*, is the visible portion of the ear which serves as a funnel to aid in the collection of sound waves.

The *external auditory canal* extends from the outer ear to the drum membrane. It is lined with fine hairs, and glands which produce

¹ This material is available in leaflet form and may be obtained by addressing the Surgeon General, U. S. Public Health Service, Washington, D. C.

sweat and wax. Through this canal sound waves and outside air pressures reach the eardrum.

The *drum membrane* conveys the vibrations produced by sound waves to the chain of delicate bones in the middle ear.

The *middle ear* is an air-filled chamber lying between the drum membrane and the internal ear. It contains the ossicles (tiny bones) and nerves concerned in the transmission of sound.

The *internal ear* contains the semicircular canals, and other organs for maintaining the body in a state of balance, and the cochlea which is concerned with the function of hearing.

The *eustachian tube* is a tiny passage which connects the middle ear with the nasopharynx, the space formed by the after part of the nose and the upper part of the throat. Normally, the eustachian tube conveys air at outside pressure to the middle ear, thus equalizing the air pressure on both sides of the drum membrane. In health, air is admitted into the middle ear through the eustachian tube by the acts of swallowing and yawning.

Conditions of the Auditory Canal.

1. *Foreign bodies in the ear.*—Foreign bodies in the outer ear canal at times cause only slight discomfort. Occasionally buttons and similar small smooth objects are removed from the ears of adults which were evidently placed in the ears during childhood. No unskilled person should attempt to remove foreign objects from the ear. Improper, rough handling frequently pushes the object more deeply into the ear and, in some cases, the drum membrane may be seriously damaged.

When an insect gets into the ear, filling the canal with tepid water or glycerin may float the insect out. If this measure fails, expert medical assistance should be secured.

2. *Ear wax.*—Ear wax in moderate amount is a normal secretion of the glands in the external ear canal. It serves as a sticky protection against the entrance of dust and crawling insects. When ear wax dries, it tends to be dislodged by the movements of the jaws. In some individuals the wax remains soft and tends to accumulate in the canal. At times the collection of wax may be so great as to interfere temporarily with hearing.

Under no circumstances should hairpins or any pointed instrument be introduced into the ear canal in an effort to remove wax. To do so may injure the lining of the canal and lead to infection. Hardened wax may be pushed farther into the canal with resulting injury to the drum membrane.

In many instances, softening the wax with glycerin, followed by gentle syringing of the ear with warm water or weak salt solution, will remove the accumulation of wax. In syringing the ear, the fluid

should be introduced slowly against the back wall of the canal and with very little pressure. After washing the ear out, the head should be turned on one side so that the excess of fluid can run out. The canal may then be wiped out with a swab of cotton to clear it of moisture which, if left in the ear, will create conditions favorable to the growth of germs. Never introduce the swab far into the ear canal.

When these simple procedures fail to remove the excess wax, a physician should be consulted.

3. *Infections.*—The auditory canal is a favorable site for the development of certain skin infections, among which boils and fungus growths are common examples.

All infections of the auditory canal should receive the attention of a physician.

Infections of Middle Ear.

Infections of the middle ear are commonly caused by such germs as the streptococcus, the pneumococcus, and the staphylococcus. Enlarged adenoid tissue in children who suffer repeatedly with colds is the outstanding predisposing cause of middle ear infections. Forceful blowing of the nose, when the nose is stopped up, and especially when upper respiratory infection is present, may force infectious material into the eustachian tube and thus toward the middle ear. Serious infection may result.

Repeated inflammations in the upper respiratory tract often cause chronic enlargement of the adenoids and tonsils. These structures may then press upon the exit of the eustachian tube and interfere with its proper ventilation and drainage. This results in a condition which increases the likelihood of infection of the middle ear.

Infection of the middle ear commonly accompanies diseases such as pneumonia, influenza, whooping cough, measles, and scarlet fever. Repeated infections of the middle ear often result in permanent impairment in hearing. It is estimated that nearly 75 percent of deafness occurs before the fifth year, and that 9 out of 10 cases of deafness occur before the age of 20.

CAUTION: Individuals with chronic discharging ears are advised to remain under the care of a physician. A discharging ear is always a danger.

Eardrum membrane and ear infections.—Uninformed persons believe that a hole in the eardrum permanently interferes with hearing, and may cause other serious damage. Because of fear of having the drum opened, some parents postpone the proper treatment of middle ear infections, even though an accumulation of pus causes the drum membrane to bulge. As a matter of fact, when eardrum perforation is

properly and promptly made by the surgeon to relieve middle ear infection, the membrane usually heals as soon as the inflammation subsides, with no impairment of hearing which can be attributed to the incision of the drum. It is less dangerous to have the physician examine the eardrum and incise it when necessary than to permit the pressure of the pus to force its way into the spaces surrounding the ear. Waiting for a perforation to take place may increase the tendency of the infection to spread into the mastoid bone, which complication is a serious condition.

Educational Aspect of Problem.

Educational authorities have long recognized the educational problem of persons suffering severe degrees of handicap from defective hearing. Most States provide institutional care for the deaf where instruction in speech and lip reading and vocational training is provided. The sign language, also known as the manual method, is gradually being replaced by more modern methods.

The standardizing of hearing tests under properly controlled conditions has enabled investigators to discover early deafness more readily. It is felt that it is better not to segregate the hard-of-hearing children but to permit them to carry on their normal education with the addition of classes in special instruction. This makes more of the normal social contacts possible.

The provision of appropriate vocational training is essential for deaf and hard-of-hearing children. It is known that the range of occupations is considerably wider than that available for the blind.

Protective Measures.

1. Maintain good bodily health. This increases resistance against disease.
2. Avoid upper respiratory infections.
3. Secure prompt medical attention for every acute infectious disease to avoid ear complications.
4. Do not blow the nose violently.
5. Keep the ear canal clean, but observe every precaution not to damage its delicate structure.
6. Diseased or chronically enlarged tonsils, and nasal growths, including enlarged adenoids, should be given prompt medical attention. Whatever interferes with the maintenance of proper air pressure within the middle ear, or drainage through the eustachian tube, seriously endangers the delicate hearing apparatus.
7. Periodic and skillful testing of the hearing of all school children, with the provision of medical attention and special instruction to those found with defective hearing.

**DO NOT INDULGE IN SELF-DIAGNOSIS OR SELF-TREATMENT. CONSULT
YOUR DOCTOR**

FLUORIDES IN FOOD AND DRINKING WATER¹

A REVIEW

The endemic tooth hypoplasia known as mottled enamel is caused by drinking waters containing toxic quantities of fluorides. Fluorides also occur in some common foods. The results of a study of the effects of water-ingested sodium fluoride as compared with food-ingested sodium fluoride are presented in this bulletin. Findings show that for the growing rat the same quantity of sodium fluoride consumed in the food may be equal in toxicity to that consumed in drinking water. An acute toxic effect may be produced in the rat by 180 p.p.m. or more of fluorine when present in the drinking water, but not when present in the food. Judging from balance studies on growing rats, fluorine retention equals about 30 to 40 percent of the intake. The majority of this retained fluorine is deposited in the bones and teeth. The degree of tooth hypoplasia due to fluorosis in the rat is directly correlated with the quantity of fluorine present, 0.03 to 0.04 percent of fluorine representing the approximate maximum quantity that may be present in the whole tooth and the tooth enamel still retain its normal macroscopic appearance.

Although it is extremely difficult to judge the actual conditions of human ingestion, an accumulation of fluorine in the bones of adults living in areas where mottled enamel is endemic may be expected. An accumulation of abnormal and perhaps pathologic quantities of fluorine in the bones of adults living in these areas is probable. Further study of chronic fluorosis requires that emphasis be placed on the deposition of ingested fluorine in bones and teeth.

COURT DECISION ON PUBLIC HEALTH

Vaccination and compulsory education.—(Pennsylvania Superior Court; *In re Marsh, Appeal of Marsh*, 14 A.2d 368; decided June 25, 1940.) At the beginning of a school year a child of good health and compulsory school age was refused admission to a free, public school and sent home because of his failure to produce a physician's certificate setting forth that he had been successfully vaccinated or had previously had smallpox. The school authorities, in refusing admission, acted under a statutory duty. Thereafter, having been sent to school by his father, the child presented himself for admission almost daily for about 6 weeks, but each time he was rejected and

¹ National Institute of Health Bulletin No. 172. Fluorides in food and drinking water. A comparison of effects of water-ingested versus food-ingested sodium fluoride. By F. J. McClure. Available from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., at 15 cents per copy.

sent home. At the end of that time a petition was filed by the school district attendance officer, in a court sitting as a juvenile court, for the production of the child on a charge of being a delinquent and neglected child. The child's father admitted his opposition to the vaccination of his son but sought to justify his unwillingness on the ground that the practice of vaccination was harmful and injurious. Also, no evidence was given at the hearing that the child was provided with any regular or systematic instruction.

The statute known as the juvenile court law included within its definition of a delinquent child one who was habitually truant from school or home and included within its definition of a neglected child one whose parent neglected or refused to provide proper or necessary education. The lower court adjudged the child to be a neglected child and committed him into the care and custody of a county child welfare service. An appeal to the superior court followed, and that court affirmed the order of the court below.

In passing on the appeal the superior court stated that the question was simply whether the child was a "delinquent" and "neglected" child within the meaning of the juvenile court law and said that the child could not reasonably be adjudged "delinquent" for the reason that the responsibility for continued absence from attendance at school could not properly be imputed to him. "It was," said the court, "the refusal and neglect of John Marsh to have his son vaccinated in accordance with the lawful requirements of the acts of 1895 and 1919 that prevented the latter's attendance at the public school." It was observed that the record contained no evidence indicating that the child was particularly unfit for vaccination or that vaccination, properly performed, was likely to result in harmful and injurious effects to him. There was quoted language from a United States Supreme Court case in which that court, in speaking of evidence in opposition to vaccination on the grounds that it was of little or no value in preventing smallpox or that it caused other diseases, said that it judicially knew that an opposite theory accorded with the common belief and was maintained by high medical authority. The view was taken that the father had the choice of permitting his son to be vaccinated and thereby qualify for admission to a public, private, or parochial school or of providing other adequate and systematic instruction, as for example, under a properly qualified private tutor, and thus avoid the requirement of vaccination. Having failed to do either, the father was deemed to have neglected or refused to provide proper or necessary education for his son.

DEATHS DURING WEEK ENDED AUGUST 3, 1940

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Aug. 3, 1940	Correspond- ing week, 1939
Data from 88 large cities of the United States:		
Total deaths.....	8,763	7,114
Average for 3 prior years.....	7,258	
Total deaths, first 31 weeks of year.....	271,522	265,776
Deaths under 1 year of age.....	556	412
Average for 3 prior years.....	497	
Deaths under 1 year of age, first 31 weeks of year.....	15,684	15,797
Data from industrial insurance companies:		
Policies in force.....	65,006,071	66,862,304
Number of death claims.....	11,753	10,339
Death claims per 1,000 policies in force, annual rate.....	9.5	8.1
Death claims per 1,000 policies, first 31 weeks of year, annual rate.....	10.0	10.6

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED AUGUST 10, 1940

Summary

As compared with the preceding week, increases are shown during the current week for influenza, poliomyelitis, and typhoid fever, while decreases are reported for diphtheria, measles, meningococcus meningitis, scarlet fever, smallpox, and whooping cough. For the current week, influenza, measles, and poliomyelitis are slightly above the 5-year (1935-39) median expectancy.

Poliomyelitis is closely following the curve of seasonal incidence. For the country as a whole, 275 cases were reported for the current week as compared with 195 last week and with a 5-year median of 261. Current increases are recorded for all geographic areas except the West South Central, Mountain, and Pacific areas, the largest numbers of cases reported and the largest numerical increases being for the East North Central (43 to 92), West North Central (47 to 61), East South Central (8 to 20), and the South Atlantic (16 to 28). The largest numbers of cases were reported in Indiana (41), Michigan (31), Kansas (26), West Virginia (20), and Iowa (19).

The incidence of influenza, though not alarmingly high, has been persistently above the 5-year median so far this year. It is higher for the current week than for any corresponding period of the past 5 years, and the total number of cases to date is higher than that for the same period for each of the 5 preceding years with the exception of 1937.

During the current week, 31 cases of Rocky Mountain spotted fever were reported in the eastern and mid-western States, while only 1 case (in California) was reported west of the Rocky Mountains. Fifty-eight cases of endemic typhus fever were reported, principally in the eastern and southern States, and 7 cases of tularaemia, of which 6 occurred in Utah.

For the current week the Bureau of the Census reports 7,210 deaths in 88 major cities in the United States, as compared with 8,763 for the preceding week and with a 3-year (1937-39) average of 7,348 for the corresponding week.

Telegraphic morbidity reports from State health officers for the week ended August 10, 1940, and comparison with corresponding week of 1939 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none were reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Med- dian, 1935- 39	Week ended—		Med- dian, 1935- 39	Week ended—		Med- dian, 1935- 39	Week ended—		Med- dian, 1935- 39
	Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939	
NEW ENG.												
Maine	0	0	0				30	5	5	0	0	0
New Hampshire	0	0	0				1	3	2	0	0	0
Vermont	0	0	0				3	10	2	0	0	0
Massachusetts	6	3	6				191	50	50	0	2	1
Rhode Island	0	0	0				11	24	1	0	0	0
Connecticut	0	1	1				7	19	16	0	0	0
MID. ATL.												
New York	8	11	11	11	14	14	288	130	202	2	3	3
New Jersey ¹	2	4	4	2	1	3	124	14	41	1	0	1
Pennsylvania	10	17	16				118	42	76	1	4	4
E. NO. CEN.												
Ohio ¹	2	3	9	4	7	4	19	16	58	1	1	2
Indiana	7	5	8	2	2	4	6	1	8	0	0	2
Illinois ¹	11	23	17	4	4	4	58	15	30	0	0	2
Michigan ¹	5	6	12	4			153	39	60	0	1	1
Wisconsin	0	2	2	19		14	141	45	61	0	0	0
W. NO. CEN.												
Minnesota	0	1	2			1	14	11	8	0	0	0
Iowa ¹	2	4	3		1	2	30	21	5	0	1	2
Missouri ¹	0	0	5			25	2	0	4	0	0	0
North Dakota	7	3	2				1	2	2	1	1	0
South Dakota	0	1	1		1		1	3	2	0	0	0
Nebraska	2	0	1				1	0	1	0	0	0
Kansas	6	3	3				14	3	3	0	0	0
SO. ATL.												
Delaware	1	0	0				0	0	1	0	0	0
Maryland ¹¹	3	1	3	4		1	5	6	6	1	1	2
Dist. of Col. ¹	1	2	2				1	8	5	0	0	0
Virginia ¹⁴	9	25	16	46	30		37	19	19	0	0	1
West Virginia ¹	0	5	5	1	4	7	5	3	3	1	0	1
North Carolina ¹⁴	6	27	22	9			14	13	13	0	1	1
South Carolina ¹⁴	4	11	8	110	121	54	7	1	5	2	1	0
Georgia ¹⁴	2	20	10	5			6	6	0	0	1	0
Florida ¹	1	2	5		5	1	4	2	2	1	0	0
E. SO. CEN.												
Kentucky	3	14	11	4	2		27	0	14	1	1	2
Tennessee ¹⁴	4	7	8	6	9	9	6	6	6	0	2	2
Alabama ¹⁴	8	17	12	3	21	11	26	4	4	2	3	1
Mississippi ¹	0	13	12					0		1	1	1
W. SO. CEN.												
Arkansas	3	7	8	4	11	7	0	0	3	0	0	1
Louisiana ¹⁴	3	2	9	3	7	7	0	4	4	0	0	0
Oklahoma	3	4	4	36	10	11	1	2	4	2	0	0
Texas ¹⁴	15	16	24	151	23	39	52	7	33	2	3	3
MOUNTAIN												
Montana	0	0	1	3			8	17	8	0	0	0
Idaho	0	0	0				0	1	3	0	1	0
Wyoming	2	1	1				2	9	4	0	0	0
Colorado	4	13	7	6	4		4	8	8	0	0	1
New Mexico	0	0	1				9	0	1	0	0	0
Arizona	1	1	1	6	7	7	9	4	4	0	1	1
Utah ¹	0	0	0				12	6	6	0	0	0
PACIFIC												
Washington	2	3	0				4	97	20	0	0	0
Oregon	0	0	1	1	1	2	25	19	11	0	1	0
California ¹⁴	10	19	17	17	4	5	62	113	99	0	2	3
Total	153	297	309	451	279	268	1,539	808	1,111	19	32	60
32 weeks	8,688	11,696	14,089	168,789	151,299	141,470	227,464	347,849	347,849	1,068	1,353	4,087

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended August 10, 1940, and comparison with corresponding week of 1939 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and para-typhoid fever		
	Week ended		Med- ian, 1935- 39	Week ended		Med- ian, 1935- 39	Week ended		Med- ian, 1935- 39	Week ended		Med- ian, 1935- 39
	Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939	
NEW ENG.												
Maine.....	1	0	0	1	2	4	0	0	0	1	3	3
New Hampshire.....	0	0	0	2	1	1	0	0	0	0	0	1
Vermont.....	0	1	1	3	1	0	0	0	0	0	1	1
Massachusetts.....	0	4	4	21	20	23	0	0	0	2	1	3
Rhode Island.....	0	1	1	0	0	3	0	0	0	0	2	2
Connecticut.....	2	3	3	4	3	6	0	0	0	3	3	1
MID. ATL.												
New York.....	4	11	11	65	71	76	0	0	0	16	10	25
New Jersey ¹	1	3	4	18	14	14	0	0	0	10	6	6
Pennsylvania.....	1	7	7	57	50	56	0	0	0	15	25	22
E. NO. CEN.												
Ohio ²	16	9	4	33	61	61	0	1	0	8	16	16
Indiana.....	41	1	1	11	24	23	0	0	0	6	8	7
Illinois ³	4	5	11	53	52	90	0	2	2	7	35	35
Michigan ⁴	31	78	14	46	72	76	0	2	1	6	20	12
Wisconsin.....	0	3	2	35	30	31	1	0	1	0	1	2
W. NO. CEN.												
Minnesota.....	1	23	4	12	22	22	5	0	1	3	2	1
Iowa ²	19	1	1	6	3	9	0	2	4	5	1	4
Missouri ²	12	1	1	13	13	15	0	0	1	19	14	26
North Dakota.....	0	1	0	3	11	5	0	0	0	5	0	0
South Dakota.....	2	0	0	4	13	5	3	1	1	0	2	0
Nebraska.....	1	2	0	5	12	4	1	1	1	1	2	0
Kansas.....	26	6	2	16	24	24	0	1	1	5	4	8
SO. ATL.												
Delaware.....	0	0	0	0	0	1	0	0	0	0	2	1
Maryland.....	1	0	1	10	16	10	0	0	0	3	12	14
Dist. of Col. ²	0	0	1	1	5	4	0	0	0	2	2	2
Virginia ^{2,4}	5	2	2	9	8	8	0	0	0	8	23	35
West Virginia ²	20	0	1	11	12	14	0	0	0	6	22	22
North Carolina ^{2,4}	2	7	6	16	32	25	1	0	0	3	13	22
South Carolina ⁴	0	14	2	1	9	5	0	0	0	10	15	18
Georgia ^{2,4}	0	3	1	7	8	6	0	0	0	23	36	26
Florida ²	0	2	2	4	2	2	0	0	0	4	5	2
E. SO. CEN.												
Kentucky.....	16	6	4	13	20	17	0	0	0	16	43	50
Tennessee ^{2,4}	3	0	1	7	14	8	0	1	0	11	35	35
Alabama ⁴	1	2	2	4	15	8	0	0	0	14	12	18
Mississippi ³	0	2	2	6	3	3	0	0	0	14	7	10
W. SO. CEN.												
Arkansas.....	1	0	0	6	8	6	0	0	0	30	20	23
Louisiana ⁴	5	0	1	1	5	5	0	0	0	14	22	19
Oklahoma.....	5	2	1	4	4	8	1	0	0	19	15	44
Texas ⁴	12	1	1	9	12	34	0	0	0	72	49	87
MOUNTAIN												
Montana.....	8	0	0	5	3	3	0	0	0	1	1	2
Idaho.....	0	0	0	2	0	3	0	0	0	0	2	1
Wyoming.....	1	0	0	3	0	2	0	1	0	1	1	1
Colorado.....	1	3	2	8	20	12	12	0	0	1	2	2
New Mexico.....	1	2	0	0	5	5	0	1	0	2	2	6
Arizona.....	0	4	0	0	2	1	0	0	0	0	1	1
Utah ²	1	0	0	5	2	7	0	0	0	3	1	1
PACIFIC												
Washington.....	16	0	0	1	9	9	0	0	1	0	0	3
Oregon.....	2	0	0	6	7	7	0	0	0	0	3	3
California ^{2,4}	12	51	20	35	39	46	1	9	4	15	4	9
Total.....	275	261	261	582	759	865	25	22	33	384	506	634
32 weeks.....	1,670	1,805	1,805	118,285	115,792	164,040	1,952	8,632	7,914	4,592	6,602	7,543

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended August 10, 1940, and comparison with corresponding week of 1939 and 5-year median—Con.

Division and State	Whooping cough		Division and State	Whooping cough	
	Week ended			Week ended	
	Aug. 10, 1940	Aug. 12, 1939		Aug. 10, 1940	Aug. 12, 1939
NEW ENG.			SO. ATL.—continued.		
Maine.....	38	15	North Carolina ^{1 4}	146	89
New Hampshire.....	0	0	South Carolina ⁴	21	35
Vermont.....	14	12	Georgia ^{1 4}	20	8
Massachusetts.....	147	77	Florida ⁴	6	3
Rhode Island.....	1	12			
Connecticut.....	25	57	E. SO. CEN.		
MID. ATL.			Kentucky.....	58	43
New York.....	343	391	Tennessee ^{1 4}	54	15
New Jersey ¹	91	180	Alabama ⁴	9	21
Pennsylvania.....	426	388	Mississippi ¹		
E. NO. CEN.			W. SO. CEN.		
Ohio ¹	243	257	Arkansas.....	18	14
Indiana.....	18	50	Louisiana ⁴	27	43
Illinois ¹	152	298	Oklahoma.....	22	1
Michigan ¹	287	248	Texas ⁴	223	58
Wisconsin.....	83	190	MOUNTAIN		
W. NO. CEN.			Montana.....	2	10
Minnesota.....	44	29	Idaho.....	7	3
Iowa ¹	42	10	Wyoming.....	5	0
Missouri ¹	31	32	Colorado.....	9	22
North Dakota.....	13	10	New Mexico.....	8	9
South Dakota.....	8	3	Arizona.....	5	6
Nebraska.....	5	13	Utah ¹	55	84
Kansas.....	50	14	PACIFIC		
SO. ATL.			Washington.....	40	13
Delaware.....	6	7	Oregon.....	30	26
Maryland ^{1 3}	118	57	California ^{1 4}	260	91
Dist. of Col. ¹	6	45	Total.....	3,302	3,096
Virginia ^{1 4}	36	99			
West Virginia ¹	50	8	32 weeks.....	103,877	123,958

¹ New York City only.

² Rocky Mountain spotted fever, week ended Aug. 10, 1940, 32 cases as follows: New Jersey, 2; Ohio, 2; Illinois, 2; Iowa, 5; Missouri, 1; Maryland, 6; District of Columbia, 2; Virginia, 7; North Carolina, 1; Georgia, 2; Tennessee, 1; California, 1.

³ Period ended earlier than Saturday.

⁴ Typhus fever, week ended Aug. 10, 1940, 58 cases as follows: Virginia, 1; North Carolina, 3; South Carolina, 3; Georgia, 21; Florida, 6; Tennessee, 1; Alabama, 11; Louisiana, 2; Texas, 8; California, 2.

WEEKLY REPORTS FROM CITIES

City reports for week ended July 27, 1940

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Data for 90 cities: 5-year average	89	25	12	722	290	303	5	356	64	1,405	-----
Current week	54	24	8	1,092	256	237	0	258	56	1,252	-----
Maine:											
Portland	0		0	3	1	0	0	0	0	4	19
New Hampshire:											
Concord	0		0	0	0	0	0	1	0	0	12
Manchester	0		0	0	0	3	0	0	0	0	8
Nashua	0		0	0	0	0	0	0	0	0	15
Vermont:											
Barre											
Burlington	0		0	0	0	0	0	0	0	0	8
Rutland	0		0	0	0	0	0	0	0	0	5
Massachusetts:											
Boston	1		0	65	10	4	0	14	2	55	184
Fall River	0		0	12	1	2	0	0	0	6	27
Springfield	0		0	4	0	1	0	2	0	0	47
Worcester	0		0	75	4	2	0	1	0	6	42
Rhode Island:											
Pawtucket	0		0	0	0	0	0	0	0	0	16
Providence	0		0	19	3	1	0	1	0	5	57
Connecticut:											
Bridgeport	0		0	2	0	0	0	0	1	1	42
Hartford	0		0	1	1	1	0	0	0	1	43
New Haven	0	2	0	1	0	3	0	0	1	12	23
New York:											
Buffalo	0		0	5	3	5	0	4	0	12	120
New York	9	4	4	250	48	32	0	81	2	141	1,465
Rochester	0		0	2	1	0	0	1	0	4	78
Syracuse	0		0	1	2	2	0	0	0	9	44
New Jersey:											
Camden	0		0	6	0	0	0	0	0	0	22
Newark	0		0	79	2	5	0	9	0	26	87
Trenton	0		0	1	2	1	0	3	3	7	35
Pennsylvania:											
Philadelphia	2	1	1	116	6	19	0	15	1	35	456
Pittsburgh	1		0	1	6	6	0	8	1	33	150
Reading	0		0	0	0	0	0	3	0	31	23
Scranton	0			0		0			0	0	
Ohio:											
Cincinnati	1		1	0	0	6	0	11	0	26	179
Cleveland	0	2	0	6	5	13	0	14	0	64	206
Columbus	0		0	0	2	2	0	4	0	35	107
Toledo	0		0	1	1	2	0	6	0	4	85
Indiana:											
Anderson	1		0	0	0	1	0	0	0	1	7
Fort Wayne	0		0	2	2	0	0	0	0	0	25
Indianapolis	1		0	2	5	2	0	4	1	3	118
Muncie	0		0	0	1	0	0	0	0	1	15
South Bend	0		0	0	0	0	0	0	0	0	13
Terre Haute	0		0	0	1	0	0	0	0	0	15
Illinois:											
Alton	0		0	0	0	1	0	0	0	0	14
Chicago	3	2	1	70	14	45	0	37	2	75	917
Elgin	0		0	2	1	0	0	0	0	4	12
Moline	0		0	0	0	0	0	0	0	0	12
Springfield											
Michigan:											
Detroit	2	1	0	139	17	17	0	24	0	138	308
Flint	0		0	0	1	0	0	0	0	13	23
Grand Rapids	0		0	19	2	2	0	0	0	20	42
Wisconsin:											
Kenosha	0		0	4	0	0	0	0	0	0	8
Madison	0		0	5	0	1	0	0	0	10	23
Milwaukee	0		0	122	2	4	0	2	0	15	139
Racine	0		0	2	0	0	0	1	0	0	12
Superior	0		0	4	0	0	0	0	0	0	8

¹ Figures for Barre, Springfield, Ill., and Wichita estimated; reports not received.

City reports for week ended July 27, 1940—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Small-pox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth.....	0		0	1	2	0	0	2	0	1	26
Minneapolis.....	0		0	1	3	3	0	0	0	14	128
St. Paul.....	0		0	2	4	1	0	0	0	15	75
Iowa:											
Cedar Rapids.....	0			1		0	0		0	2	
Davenport.....	0			0		1	0		0	0	
Des Moines.....	0		0	1	0	0	0	0	0	0	60
Sioux City.....	0			0		0	0		0	1	
Waterloo.....	0			1		0	0		0	2	
Missouri:											
Kansas City.....	2		0	2	1	2	0	3	0	4	87
St. Joseph.....	0		0	0	3	0	0	2	1	0	35
St. Louis.....	0		0	2	5	7	0	12	21	32	224
North Dakota:											
Fargo.....	0		0	0	0	0	0	0	0	2	4
Grand Forks.....	0			0		1	0		0	2	
Minot.....	0		0	0	0	0	1	0	0	1	18
South Dakota:											
Aberdeen.....	0			2		0	0		0	2	
Sioux Falls.....	0		0	0	0	0	0	0	0	0	7
Nebraska:											
Lincoln.....	0			1		0	0		0	0	
Omaha.....	0		0	2	3	1	0	1	0	1	68
Kansas:											
Lawrence.....	0		0	0	0	0	0	0	0	0	1
Topeka.....	0		0	0	2	1	0	1	0	2	17
Wichita.....											
Delaware:											
Wilmington.....	0		0	1	3	1	0	2	0	0	25
Maryland:											
Baltimore.....	1		0	1	8	3	0	9	1	126	236
Cumberland.....	0		0	0	0	0	0	0	0	0	14
Frederick.....	0		0	0	0	0	0	0	1	0	6
Dist. of Col.:											
Washington.....	2		0	2	13	4	0	19	0	17	224
Virginia:											
Lynchburg.....	3		0	0	0	0	0	0	0	0	9
Norfolk.....	0		0	1	1	2	0	0	0	1	27
Richmond.....	0		0	1	1	0	0	1	0	0	72
Roanoke.....	0		0	3	0	1	0	0	0	2	21
West Virginia:											
Charleston.....	1	1	0	0	0	0	0	0	0	0	10
Huntington.....	1			0		3	0		0	0	
Wheeling.....	0		0	5	0	0	0	1	0	1	17
North Carolina:											
Gastonia.....	0			0		0	0		0	0	
Raleigh.....	0		0	0	3	0	0	0	0	1	19
Wilmington.....	0		0	0	1	0	0	0	0	1	17
Winston-Salem.....	0		0	0	0	0	0	3	0	6	13
South Carolina:											
Charleston.....	0	1	0	0	3	1	0	2	0	0	28
Florence.....	0		0	0	1	0	0	1	2	0	5
Greenville.....	0		0	0	3	0	0	0	0	0	20
Georgia:											
Atlanta.....	2		0	0	2	1	0	3	0	2	79
Brunswick.....	0		0	0	0	1	0	0	0	0	4
Savannah.....	0	4	0	0	0	0	0	3	0	0	25
Florida:											
Miami.....	0	1	0	0	0	0	0	1	1	0	29
Tampa.....	0		0	0	1	0	0	1	0	0	20
Kentucky:											
Ashland.....	0		0	0	1	0	0	0	0	0	8
Covington.....	0		0	1	0	0	0	0	0	0	17
Lexington.....	0		0	25	0	0	0	2	0	2	14
Louisville.....	0		0	1	3	3	0	2	0	30	65
Tennessee:											
Knoxville.....	0		0	7	0	0	0	0	0	0	29
Memphis.....	0		1	4	0	0	0	6	2	7	74
Nashville.....	1		0	0	3	1	0	0	3	32	44
Alabama:											
Birmingham.....	0	1	0	2	5	3	0	3	1	0	75
Mobile.....	0		0	0	0	2	0	0	0	3	29
Montgomery.....	0			0		0	0		0	0	

City reports for week ended July 27, 1940—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Small-pox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Arkansas:											
Fort Smith.....	0			0		0	0		0	0	
Little Rock.....	0		0	0	5	0	0	1	0	6	
Louisiana:											
Lake Charles.....	1		0	0	2	0	0	0	2	2	9
New Orleans.....	0		0	1	14	2	0	11	2	4	176
Shreveport.....	0		0	0	1	3	0	0	0	0	46
Oklahoma:											
Oklahoma City.....	0	3	0	0	1	2	0	0	0	0	40
Tulsa.....	0		0	0	2	0	0	2	0	20	28
Texas:											
Dallas.....	1		0	6	0	1	0	1	2	7	72
Fort Worth.....	0		1	5	4	1	0	3	5	6	36
Galveston.....	0		0	0	1	0	0	0	0	0	18
Houston.....	4		0	0	2	0	0	4	5	6	87
San Antonio.....	1		0	0	3	1	0	2	1	14	75
Montana:											
Billings.....	0		0	0	1	0	0	0	0	0	16
Great Falls.....	0		0	4	1	0	0	1	0	0	12
Helena.....	0		0	0	0	0	0	0	0	0	4
Missoula.....	0		0	0	2	1	0	0	0	0	7
Idaho:											
Boise.....	0		0	1	0	0	0	0	0	0	2
Colorado:											
Colorado Springs.....	0		0	0	0	0	0	0	0	0	7
Denver.....	8		0	3	3	1	0	4	0	1	80
Pueblo.....	1		0	1	3	0	0	2	0	0	14
New Mexico:											
Albuquerque.....	0		0	1	1	0	0	0	1	1	12
Utah:											
Salt Lake City.....	0		0	12	0	1	0	0	0	34	22
Washington:											
Seattle.....	0		0	3	2	4	0	5	0	16	99
Spokane.....	0		0	0	0	3	0	0	0	0	28
Tacoma.....	0		0	0	1	1	0	2	1	2	25
Oregon:											
Portland.....	1		0	3	2	1	0	2	0	3	73
Salem.....	0		0	0		0	0		0	2	
California:											
Los Angeles.....	5	5	0	14	5	9	0	7	1	64	319
Sacramento.....	2		0	1	1	0	0	0	0	10	27
San Francisco.....	0		0	2	1	2	0	4	0	34	154

State and city	Meningitis, meningococcus		Polio-myelitis cases	State and city	Meningitis, meningococcus		Polio-myelitis cases
	Cases	Deaths			Cases	Deaths	
New York:				Oklahoma:			
New York.....	3	0	4	Oklahoma City.....	3	0	0
Ohio:				Tulsa.....	0	0	1
Cleveland.....	0	0	5	Texas:			
Illinois:				Fort Worth.....	0	0	1
Alton.....	0	0	1	Houston.....	0	0	2
Chicago.....	1	0	0	Montana:			
Missouri:				Missoula.....	0	0	1
St. Joseph.....	1	0	0	New Mexico:			
District of Columbia:				Albuquerque.....	0	0	1
Washington.....	1	1	0	Washington:			
West Virginia:				Seattle.....	0	0	3
Huntington.....	0	0	3	Spokane.....	0	0	1
Alabama:				Tacoma.....	0	0	9
Birmingham.....	1	0	0	California:			
Louisiana:				Los Angeles.....	0	0	2
New Orleans.....	0	0	1				
Shreveport.....	0	1	1				

Encephalitis, epidemic or lethargic.—Cases: Chicago, 1; Washington, D. C., 1; Sacramento, 3.

Pellagra.—Cases: Charleston, S. C., 1; Memphis, 1; Birmingham, 1; New Orleans, 1.

Typhus fever.—Cases: New York, 1; Savannah, 4; Miami, 2; Birmingham, 1; Montgomery, 1; New Orleans, 1; Fort Worth, 1.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended July 6, 1940.—During the week ended July 6, 1940, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brun- swick	Que- bec	On- tario	Mani- toba	Sas- katch- ewan	Alber- ta	British Colum- bia	Total
Cerebrospinal meningitis				1	5					6
Chickenpox		6	11	66	301	31	46	13	34	508
Diphtheria				14	2	3				19
Dysentery				11					2	13
Measles	1	29	4	41	116	76	193	13	38	511
Mumps				10	119	1	5		10	145
Pneumonia		5			19				3	27
Poliomyelitis				1	1					2
Scarlet fever		3	4	54	78	5		9	1	154
Tuberculosis	6	11	15	98	67	6	1			204
Typhoid and paraty- phoid fever				7	8		2	2		19
Whooping cough		14	8	164	75	9	22	15	16	323

CUBA

Habana—Communicable diseases—4 weeks ended June 1, 1940.—During the 4 weeks ended June 1, 1940, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Diphtheria	9		Scarlet fever	2	
Malaria	2		Typhoid fever	55	8

PANAMA CANAL ZONE

Notifiable diseases—April-June 1940.—During the months of April, May, and June 1940, certain notifiable diseases, including imported cases, were reported in the Panama Canal Zone and terminal cities as follows:

Disease	April		May		June	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Chickenpox.....	10		7		4	
Diphtheria.....			9		8	
Dysentery (amoebic).....		1	8		3	
Dysentery (bacillary).....		2	5	1	4	
Leprosy.....			1		1	
Malaria.....	69	2	138	3	327	1
Measles.....	1		5			
Mumps.....			3		3	
Meningococcus meningitis.....	1					
Paratyphoid fever.....			4			
Pneumonia.....		25		20		18
Scarlet fever.....					1	
Trachoma.....			1			
Tuberculosis.....		25		38		25
Typhoid fever.....	2			1	1	
Typhus fever.....			1			

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—A cumulative table giving current information regarding the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS of July 26, 1940, pages 1367-1370. A similar table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

India—Karachi.—During the week ended July 20, 1940, 10 cases of cholera were reported in Karachi, India.

Plague

Argentina.—Plague has been reported in Argentina, by Provinces, as follows: May 1940—Cordoba, 3 cases; Jujuy, 1 case; Santiago del Estero, 8 cases, 1 death; Tucuman, 1 case, 1 death. June 1940—Cordoba, 18 cases, 16 deaths, including 11 fatal cases of pneumonic plague; Santiago del Estero, 10 cases, 1 death; Tucuman, 1 suspected case. Plague among rodents has also been reported in Santiago del Estero and Tucuman Provinces.

Hawaii Territory—Island of Hawaii—Hamakua District—Paauhau Mauka Camp.—Two rats found on July 9 and July 13, respectively, in Paauhau Mauka Camp in the vicinity of Paauhau, Hamakua District, Island of Hawaii, T. H., have been proved positive for plague.

Peru.—During the month of May 1940, plague was reported in Peru, by Departments, as follows: Cajamarca, 6 cases; Lambayeque, 1 case; Libertad, 1 case, 1 death; Lima, 5 cases, 1 death; Tumbes, 10 cases, 2 deaths. There were also 21 unconfirmed suspected cases of plague reported in Tumbes Department.

Senegal—Tivaouane.—During the period June 20-30, 1940, 3 cases of plague were reported in Tivaouane, Senegal.